EVALUATION OF NIFEDIPINE TOCOLYSIS IN PRETERM LABOUR

A Dissertation Submitted to

THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY

CHENNAI

In Partial Fulfillment of the Regulations

for the Award of the Degree of

M.S. (OBSTETRICS & GYNAECOLOGY) - BRANCH – II

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CHENNAI -600 001.

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CERTIFICATE

This is to certify that this dissertation entitled “Evaluation of Nifedipine Tocolysis in Preterm labour ’submitted by DR.R SUGANTHA, appearing for Part ll MS, Branch II Obstetrics and Gynaecology Degree Examination in April 2014, is a **bonafide** record of work done by her under my direct guidance and supervision as per the rules and regulations of the Tamil Nadu Dr. MGR Medical university, Chennai, Tamil Nadu, India .I forward this dissertation to the Tamil Nadu Dr. MGR Medical University Chennai, India.

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ACKNOWLEDGEMENT

“Teacher is neither an anchor to hold you back

Nor a soil to take you there;

But a leading light whose love

Shows you the way”

I start in the name of God who is kind enough to bestow so upon me the courage, patience and perseverance throughout the course of this thesis. At the onset it seems a difficult task, a distant dream, but once it gets going, if the guidance is acuminous, if the encouragement is constant and if the support is untiring the destination becomes achievable.

The feeling of gratitude when expressed in words is only its half acknowledgement. At completion when I see through my journey I find I was lucky to get all these things at their best and from the best people. Though I will remain indebted to all those who have made this task accomplished I take this opportunity to express my gratitude to my mentors, patrons and colleagues who made an uphill task, a distant dream into reality.

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I am extremely thankful to my Assistant Professors for their valuable suggestions and help. I also thank my colleagues for their help and support. Last but not the least; I extend my sincere thanks to all my patients who willingly volunteered to be included in the study.

DECLARATION

I Dr. R. SUGANTHA, solemnly declare that the dissertation titled, **EVALUATION OF NIFEDIPINE TOCOLYSIS IN PRETERM LABOUR** is a bonafide work done by me at R.S.R.M. Lying in Hospital, Stanley Medical College, and Chennai during September 2012 – September 2013 under the

guidance and supervision of **Prof. Dr. V. KALAIVANI M.D., D.G.O.,** Professor and Chief of the department of Obstetrics and Gynaecology.

This dissertation is submitted to the Tamilnadu Dr. M.G.R. Medical University in partial fulfilment of University rules and regulations for the award of M.S. Degree (Branch-II) in obstetrics and Gynaecology.

Place: Chennai
Date: 24-12-2013

Dr. R. SUGANTHA,

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CONSENT FORM

1) I agree to participate in the study entitled '**EVALUATION OF NIFEDIPINE TOCOLYSIS IN PRETERM LABOUR'**

2) I confirm that I have been told about this study in my mother tongue and have had the opportunity to ask questions.

3) I understand that my participation is voluntary and I may refuse to participate at any time without giving any reasons and without affecting my benefits.

4) I agree not to restrict the use of any data or results that arise from this study.

Name of the participant:

Sign /Thumb print:

Sign of the Investigator:

INSTITUTIONAL ETHICAL COMMITTEE,
STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : Evaluation of Nifedipine tocolysis in preterm labour

Principal Investigator : Dr.R.Sugantha

Designation : PG in M.D (OG)

Department : Department of OG
Government Stanley Medical College,
Chennai-1

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 07.02.2013 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

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5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

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MEMBER SECRETARY,
IEC, SMC, CHENNAI

ABSTRACT

EVALUATION OF NIFEDIPINE TOCOLYSIS IN PRETERM LABOUR

AIM OF THE STUDY

1. To evaluate the Tocolytic effects of Calcium channel blocker – NIFEDIPINE in preterm labour
2. To study the maternal and fetal effects of NIFEDIPINE.
3. To compare the efficacy of Nifedipine with control group in delaying delivery for 48 hours in idiopathic spontaneous preterm labour

MATERIALS AND METHODS

STUDY DESIGN

It is prospective study conducted in Government RSRM Lying in Hospital, Stanley Medical College, Chennai , from September 2012 to September 2013 The study population comprised of patients who attended the casuality or outpatient department. There were 100 patients in Nifedipine group and 2 patients were lost to follow-up. There were 100 patients in Control group and 3 patients were lost to follow up. Study group received Nifedipine and control group were observed with bed rest. Both groups received intra muscular corticosteroids.written informed consent obtained.

DRUG PROTOCOL

GROUP A

Tab. Nifedipine 20 mg was given orally. If uterine contractions persisted after 90 minutes another 10 mg dose given. If the dosage suppressed uterine activity then maintenance of 10 mg given 6^{th} hourly for 3 days. Dosage is gradually tapered and stopped.

GROUP B

Patients observed with bed rest

Both the groups given intramuscular corticosteroids

Success and Failure

There are several studies by various authors suggesting several factors for assessment of success of tocolysis.

In our study, successful tocolysis was defined as the delay of delivery with suppression of contractions for more than 48 hours from initiation of therapy.

Failure of therapy is said to occur, when patient delivered within 48 hours of initiation of therapy and tocolysis was stopped when cervical dilatation progressed to > 3 cm or when there was spontaneous rupture of membranes.

Hence our study is confined to idiopathic spontaneous preterm labour and comparing the efficacy of Nifedipine with that of control in delaying delivery for 48 hours and regarding the maternal and fetal effects of Nifedipine.

SUMMARY

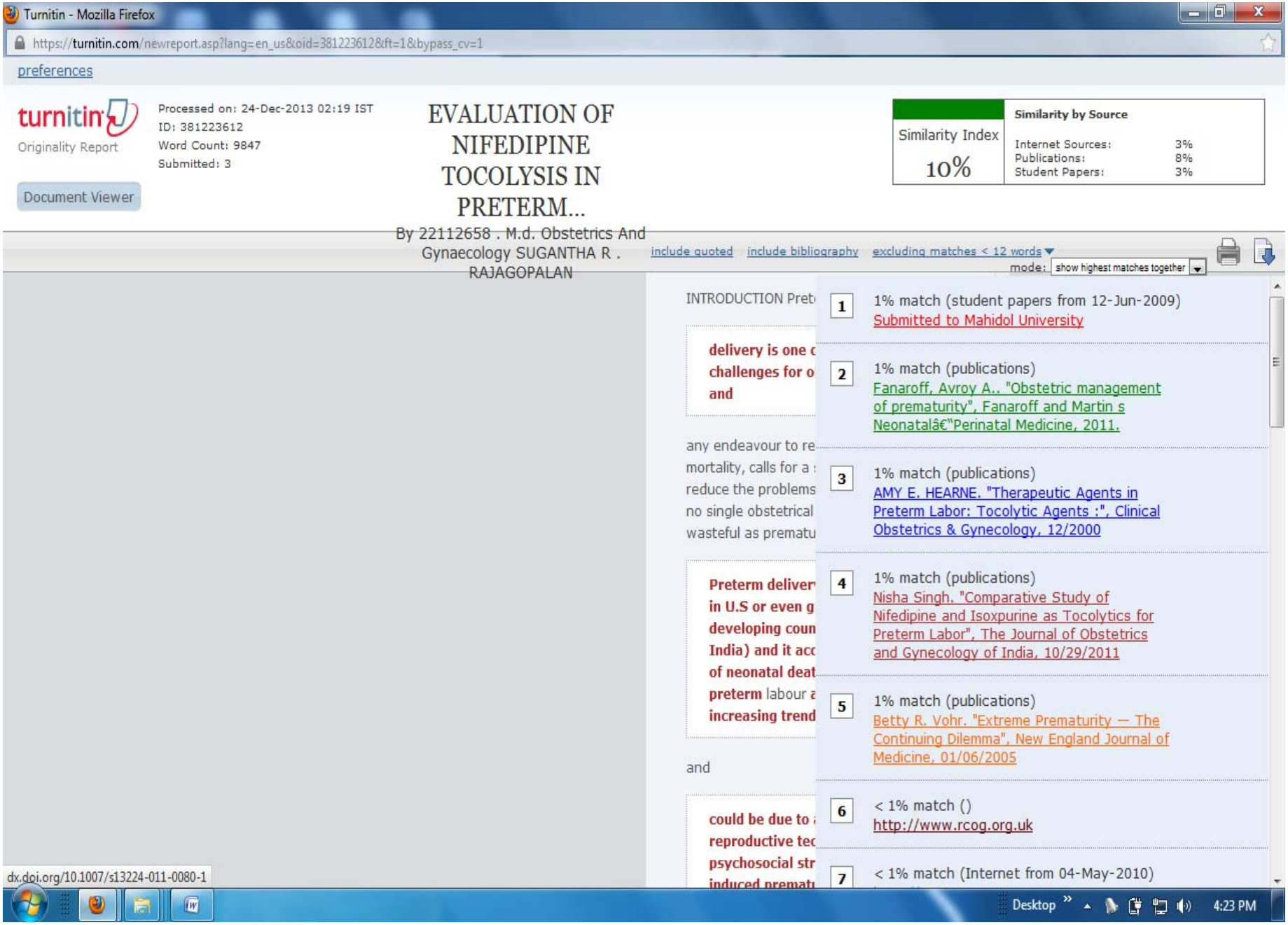
The success of Nifedipine as indicated by prolongation of pregnancy beyond 48 hours was observed in 73.4% of cases compared with 57% in controls P value was significant (< 0.001).78.57% of patients required 30 mg to suppress uterine contractions whereas 21.4% required 20 mg to stop contractions. The prolongation of pregnancy more than 48 hours was found to be more in 31 -34 weeks of gestational age in Nifedipine and control groups. About 56.1% of patients in Nifedipine group had side effects which were reversed on discontinuation Headache ,maternal tachycardia were the common side effects. There was no maternal mortality. About 11.1% and 38.46% of neonatal complications occurred in Nifedipine success and failure groups respectively. About 34.37 % and 21.5% of Neonatal complications occurred in control success and failure groups. When compared with 56.2% in control success group. 8.3% in Nifedipine success group had birth weight > 2.5kg compared to 6.5%in control success group P value 0.001 statistically significant. Incidence of Respiratory Distress syndrome is 2.7 % and 15.38% in Nifedipine success and Failure respectively compared to 12.5% and 16.9% in control success and failure groups P value is Significant (0.042)

CONCLUSION

Labour inhibiting drugs may not treat the cause of preterm labour but they only treat the symptoms, that is contractions.

These agents make the uterus refractory to contractile stimuli for a short time so that the perinatal outcome is improved.

Key words – nifedipine ,tocolysis, preterm labour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INTRODUCTION

Preterm labour and delivery is one of the biggest challenges for obstetricians and any endeavour to reduce the prenatal mortality, calls for a successful effort to reduce the problems of preterm birth, for no single obstetrical misfortune is more wasteful as prematurity.

Preterm delivery affects 11% in U.S or even greater in developing countries (23.3% in India) and it accounts for 40-75% of neonatal deaths. Incidence of preterm labour and delivery show increasing trends and could be due to assisted reproductive techniques, psychosocial stress or medically induced prematurity. Improvement in neonatal care has remarkably improved preterm survival. There is increased focus to early preterm births <32 weeks which account for 1-2% of all births; but contribute to 60% of perinatal mortality and nearly all neurological morbidity.

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Rush et al reported that 75% of neonatal deaths occurred in infants with gestational age between 32 and 37 weeks accounting for majority of neonatal deaths and nearly one half of all cases of congenital neurologic disability.

The social and emotional cost of penatal mortality and morbidity associated with preterm birth is immeasurable .Ideally preterm labour should be prevented .With improved neonatal services greater degrees of prematurity are still compatible with full and subsequently normal development.

Pharmacological methods of inhibition of preterm labour remains the most effective means to delay delivery and improve neonatal outcome till a more effective means of prevention is identified .In many instances, delaying delivery till the fetus is sufficiently mature is a tremendous gain for the fetus at no disadvantage to the mother. All that we have achieved so far is the possibility of gaining a few days with use of tocolytic agents. Our study is concerned with the Efficacy of Nifedipine – a calcium channel blocker as a tocolytic agent.

REVIEW OF LITERATURE

DEFINITION

Preterm labour is defined by the WHO as the onset of labour prior to the completion of 37 weeks of gestation in a pregnancy beyond 20 weeks of gestation.

Preterm labour is defined as the onset of regular, painful, frequent, uterine contractions causing progressive effacement and dilatation of cervix occurring before 37 completed weeks from the first day of last menstrual period.

(Anderson 1977)

THRESHOLD OF VIABLITY

Births before 26 weeks, especially those weighing less than 750 g are at the current threshold of viability and these preterm infants pose a variety of complex medical, social and ethical considerations (ACOG, 2002, 2008).

According to current guidelines of American Academy of Pediatrics (Braner, coworkers 2008) it is considered appropriate not to initiate resuscitation for infants younger than 23 weeks or birth weight less than 400g these infants are described as fragile and vulnerable because of their immature

organ systems (Vohr and Allen,2005).

Overall 25 percent of infants born at 22 to 25 weeks had severe neurological disability and 72 percent exhibited learning disability. Active brain development

normally occurs throughout the second and third trimesters, those infants born at 22 to 25 weeks are especially vulnerable to brain injury because of extreme immaturity.

Tyson and associates (2008) reported female gender, singleton pregnancy, corticosteroids given for lung maturation and higher gestational age improved the prognosis of infants born at the threshold of viability.

MC Intire and Leveno, 2008 reported that 80 percent of late preterm births were due to idiopathic spontaneous preterm labour or prematurity ruptured membranes. Complications such as hypertension or placental accidents were implicated in approximately 20% of cases.

PETRINI and co-workers, 2009, reported the increased rates of adverse neurodevelopment in late preterm infants compared with term newborns. Fuchs and colleagues (2009) reported respiratory morbidities in preterm infants.

PROBLEMS OF PRETERM BIRTH

Apart from survival, appreciable physical and intellectual compromise afflicts preterm infants. Eichenwald and Stark (2008) studied extensively on short term and long term complications of preterm infants.

SHORT TERM COMPLICATIONS

- Respiratory Distress Syndrome
- Bronchopulmonary dysplasia
- Apnea of prematurity
- Hyperbilirubinemia
- Necrotising enterocolitis
- Immune deficiency
- Intraventricular haemorrhage
- Periventricular leukomalacia
- Retinopathy of prematurity
- Hypotension
- Patent Ductus Arteriosus
- Pulmonary hypertension
- Anemia of prematurity
- Hypoglycaemia, cortisol deficiency

LONG TERM COMPLICATIONS

- ❖ Reactive Airway Disease
- ❖ Asthma
- ❖ Failure to thrive
- ❖ Short bowel syndrome
- ❖ Cholestasis
- ❖ Respiratory syncytial virus infections
- ❖ Bronchiolitis
- ❖ Cerebral palsy
- ❖ Neuro developmental delay
- ❖ Hearing loss
- ❖ Blindness
- ❖ Retinal detachment
- ❖ Myopia, Strabismus
- ❖ Pulmonary Hypertension
- ❖ Hypertension in adulthood
- ❖ Impaired glucose regulation
- ❖ Increased insulin resistance

A wide spectrum of causes and demographic factors have been implicated in preterm birth .Preterm labour, preterm ruptured membranes, preeclampsia,

abruption placenta, multiple gestations, placenta praevia, fetal growth restrictions, excessive or inadequate fluid volume, fetal anomalies, amnionitis, incompetent cervix, as well maternal medical problems such as diabetes mellitus, asthma, drug abuse and pyelonephritis may lead to preterm delivery.

PATHOGENESIS OF PRETERM LABOUR

Preterm labour can be physiological process occurring prematurely or a process which is pathological occurring due to an abnormal stimulus.

Aetiology of preterm labour may be multifactorial but evidence of infection as an important cause of preterm labour is mounting. The earlier the onset of labour the more likely infection is implicated.

Progesterone withdrawal theory in the process of parturition has been well understood in sheep but has not been clearly implicated in us. The reversal of the ratio of estrogen - progesterone has resulted in increased synthesis of prostaglandins and the subsequent initiation of parturition.

The molecular basis of initiation of labour is unclear but a number of theories have been implicated.

Progesterone withdrawal, oxytocin stimulation and premature decidual activation are important. Regardless of the stimulus the final pathway seems to converge towards a central role of inflammatory mediators – CYTOKINES.

Intra amniotic infections can induce the activation of chemokines and variety of cytokines which in turn induce cervical softening, pre term rupture of membranes and pre term labour. There is a recruitment of WBC ‘S in response to an inflammation resulting from infection which can subsequently undergo activation triggering pre term contractions. There is evidence of increased levels of

cytokines in the amniotic fluid in patients with pre term labour having evidence of infections. These women who have documented evidence of amniotic infection are known to be refractory to treatment with tocolytics

Progesterone inhibitors (mifepristone) have been implicated in the formation of cascade of inflammatory mediators which trigger labour. The present concept of the role of the hormone progesterone in preventing the occurrence of pre term labour has been investigated.

Though oxytocin hormone is considered to be vital for the induction of labour, its role is negligible in the natural process because neither their levels increase before parturition nor their levels decrease with advancement of pregnancy.

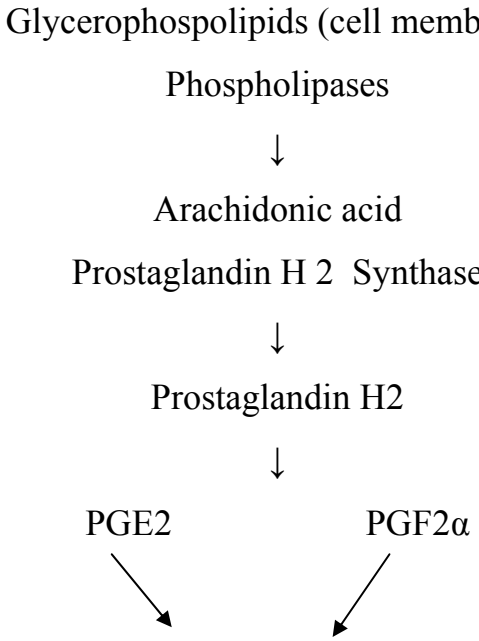
Csapo (1961) proposed the progesterone block theory to explain the onset of labour. According to him; labour was initiated when the delicate balance between myometrial relaxant (progesterone) and myometrial stimulant (estrogen) was altered in favour of the latter.

Differential production of PGE2 and PGF2 α by the three enzymes phospholipases, PGH2 synthase, and 15 hydroxy prostaglandin dehydrogenase maintains the balance between uterine activity and quiescence. The decidual activation and production of uterotropins initiate parturition (Skinner and Challis, 1985)

When fetal adrenal axis becomes more sensitive to ACTH, there is increase in cortisol production, leading to increased 17 hydroxylase and finally decreased progesterone.

Cox and colleagues (1993) found that cytokines (IL1,IL6,TNF alpha ,IL8 are released when there is inflammatory response to infection and intra uterine bleeding. These in turn stimulate arachidonic acid and prostaglandin production.

Whatever the mechanism to initiate labour, three physiological processes have to occur namely softening and dilatation of the cervix, uterine myometrial contraction and weakening and rupture of membranes.



MYOMETRIAL CONTRACTION

ROLE OF CYTOKINES IN PRETERM LABOUR

Interleukin , 6 and 8, and Tumour necrosis factor alpha are involved in the dissolution of the collagen fibres and cause cervical softening. Ruptures of membranes induced by the matrix metallo proteinases are caused by inter leukin 1 and Tumour necrosis factor alpha.

Inter leukin 1, 2 and 6 cause an increase in prostaglandin concentration and induced uterine contractions.

Infection is implicated in 40-50% of cases of preterm labour at early weeks <30 weeks Holst RM (2005.). Infection induces an inflammatory response involving the activation of a number of cytokines and chemokines which in trigger preterm contractions, cervical ripening and rupture of membranes.

Women with documented intra amniotic infection are often refractory to tocolytics. Lamont RF (2003). Preterm babies exposed to cytokines in utero are more likely to have lung and brain damage causing bronco pulmonary dysplasia, peri ventricular leucomalacia and cerebral palsy YoonBH 2003.

Increased association between clinical infection and histological amniotic infection has been found in women with pre term labour. Both positive membrane cultures and increased concentration of the interleukin 6 has occurred in pre term labour which has occurred spontaneously. Offenbacher et al has found strong association of pre term birth with periodontal infections. Retrospective studies conducted on antenatal women who had been treated with anti microbial agents have shown to reduce the incidence of pre term delivery. The prospective trial conducted in women who had been given antibiotics after a previous pre term labour has shown decreased incidence of pre term delivery. (Mcdonald et al 1997.)

Carey et al 2000 in his study on pre term labour and antibiotics treatment reported an increased rate of pre term birth in women who were randomized to get

metro nidazole. These trials emphasize the complexity of infection and pre term labour which is explained by ascending infection which occurs in the antenatal period. Host defense mechanisms were also implicated in the causation of pre term delivery.

REASONS FOR PRETERM DELIVERY

THE FOUR MAIN DIRECT REASONS FOR PRETERM BIRTHS

1. Delivery for maternal or fetal indication in which labour is induced or the infant is delivered by pre labour caesarean delivery.
2. Spontaneous unexplained preterm labour with intact membranes
3. Idiopathic preterm premature rupture of membranes
4. Twins and higher order multi fetal births Goldenberg RL (2002)

Of Preterm births 30 to 35 percent are indicated, 40-45 percent are due to spontaneous preterm labour and 30 to 35 percent follow preterm rupture of membranes (Goldenberg and colleagues 2008b)

Medical and obstetrical Indications

Ananth and Vintzileos (2006) analysed factors leading to indicated birth before 35 weeks.

COMMON INDICATIONS FOR MEDICAL INTERVENTION RESULTING IN PRETERM LABOUR

- Preeclampsia
- Fetal distress
- Small for gestational age
- Abruptio placenta
- Less common causes
- Chronic hypertension
- Placenta praevia
- Diabetes
- Renal disease
- Rh isoimmunization
- Congenital malformation

ETIOLOGY OF PRETERM LABOUR

About 50 -60% preterm births occur following spontaneous labour, 30% is due to preterm rupture of membranes and rest are iatrogenic.(Goldenberg RL 2002; Leitich H 2006).

Meis and colleagues 1996 analyzed the causes and found that one third were indicated deliveries for maternal and fetal benefit.

One of the major reasons for preterm birth is increase in multiple pregnancies (fertility drugs and artificial reproductive techniques and increased surveillance and intervention in high risk pregnancies (Ian Doland 6th edition). Multifetal gestation has a greater risk for almost every obstetric complication that could occur ,and preterm labour is one the common problems encountered .There has been a report of triplet gestations being managed conservatively having a mean gestational age of 31 weeks.

INFECTION

1. UTERINE

Ledger and Bobitt first suggested that unrecognized chorio amnionitis may be causally related to preterm labour. They documented positive cultures via trans cervical needle aspiration or intrauterine catheters. As many as 50% of spontaneous preterm births may be associated with infection (Klein LL, Gibbs RS 2005) the common pathway of intra uterine infection is the ascending route.

Colonization of genital tract with group B Streptococcus infection is associated with preterm labour. (Bobitt and al Lamont et al).Very often Group B streptococcus has been related to the causation of preterm labour and preterm rupture of membranes. The current recommendation is to screen high risk women and to treat with antibiotics.

Colonization with Chlamydia trachomatis (Martin et al, Harrison et al) Mycoplasma hominis and urea plasma urealyticum (Klein et al 2008) is associated with preterm labour

Asymptomatic bacterial vaginosis and trichomonas vaginalis infection confers modest risk of preterm labour. Bacterial vaginosis (Gravett et al) has association with low birth weight.

Edward et al, reported higher incidence of positive gonorrhea culture in preterm labour

Presence of infection in the genital tract either as a result of overgrowth of normal bacterial flora or abnormal vaginal flora at 26-32 weeks gestation has been shown to be associated with preterm labour (Kiss et al 2004.)

23 percent of neonates born between 23 and 32 weeks have positive umbilical blood cultures for genital mycoplasmas (Goldenberg and collegues 2008 a) Morency and Bujold (2007) suggested that antimicrobials given in second trimester prevent subsequent preterm birth.

Bacterial Vaginosis

In this condition, normal hydrogen peroxide producing, lactobacillus predominant vaginal flora is replaced with anaerobes such as Gardnerella vaginalis and Mycoplasma hominis.The main complaints of bacterial vaginosis is thin watery vaginal discharge with fishy odour.,though majority of women remain asymptomatic.There has been contradictory studies reporting the beneficial effects of screening the women belonging to low and high risk groups.There are some studies implicating the cytokine production and subsequent activation of the cervix and membranes due to bacterial vaginosis.

Environmental factors have been associated with the development of bacterial vaginosis. Exposure to chronic stress, ethnic differences, and frequent or recent douching have been associated with increased rates of the condition (Culhane and workers2002; Ness and associates 2002)

Condition shown to increase preterm delivery (Flynn et al 1999) risk appears to be almost double when detected in early pregnancy (21 percent) compared to later in pregnancy (Joesoef at al 1993; Leitich et al 2003)

Hillier 1995; Kurki 1992, Leitich 2003 proved association of bacterial vaginosis with spontaneous abortion, preterm labour, preterm rupture of membranes and chorioamnionitis.

A gene environment interaction was identified by Macones and colleagues 2004. Women with bacterial vaginosis and susceptible TNF-A genotype had a ninefold increased incidence of preterm birth

However Okun and associates (2005) in their systematic analysis on use of antibiotics given for bacterial vaginosis found no supporting evidence to prevent preterm labour in either low risk or high risk women.

EXTRAUTERINE

Robertson et al (2008) reported high prematurity rate with asymptomatic bacteruria

Systemic illness like pneumonia, pyelonephritis, and periodontal disease is associated with preterm labour (Xiong X 2006).Appendicitis has also been implicated in the causation of preterm labour as stated by some studies. Oral bacteria and periodontal infection have been found to be present in women developing preterm delivery.

Vergnes and Sixoci (2007) reported a strong association between periodontal disease and preterm birth. Golpfert (2005) in his study found an increased incidence of preterm labour in patients having periodontal infection.

1. PLACENTAL

- Abnormal placentation
- Anatomical abnormalities
- Placenta praevia
- Abruptio placenta

2. UTERINE

- Congenital abnormalities 1-3% especially septate and bicornuate uterus
- In competent cervix and cervical anatomical abnormalities
- Over distension of uterus

Multifetal gestation is said to be linked with the occurrence of preterm labour. Premature uterine contractions are said to occur due the premature activation of the gap junctions, prostaglandin production and collagenase activity occurring in these conditions. The raised levels of the hormone relaxin, transfer of infections during instrumentation of the cervix are some factors relating to the occurrence of preterm labour, in assisted reproductive techniques.

The occurrence of uterine anomalies is generally less than one percentage.

Michalas 1991; Raga 1997 reported any structural anomaly that alters the uterine cavity is likely to cause miscarriage, preterm labour or mal presentation of fetus.

3. GENETIC

Genetic factors have a pivotal role in the occurence of preterm delivery.

Gibson, 2007; Hampton, 2006; Li 2004; Macones, 2004 reported literature on genetic variants causing preterm labour.

Varner and Esplin, 2005 implicated immune regulatory genes in potentiating chorio amnionitis in preterm labour.

Genes for deicidual relaxin/ fetal mito chondrial tri functional protein defects, IL-1, β2 adrenergic receptor gene, Tumour Necrosis Factor α are implicated in preterm rupture of membranes culminating in preterm delivery.

Vaginal bleeding in early pregnancy is associated with preterm labour (Williams's obstetrics 22nd edition)

4. Fetal

Dolan and colleagues (2007) reported that birth defects were associated with preterm birth and low birth weight

5. Preterm labour of unknown origin (20-30%).

About 20 -30 % of preterm deliveries occur without any demonstrable etiology.

EPIDEMIOLOGY

1 RACE

Goldenberg and colleagues 2008 reported higher risk of preterm birth in Black, African – American and Afrocaribbean.

Black women have increased risk for recurrent preterm birth (Kistka and Colleagues, 2007) African American women have an increased rate of pre term

deliveries when compared to other races as stated by the Center for Health statistics

In 1996 Genc reported that social and demographic factors did not influence the rate of pre term birth in African American women.(2000)

2. AGE

Preterm labour is more common in extremes of age .Lumley JM et al 1993 reported high incidence of preterm delivery in women under 17 years and over 35 years.

3. WEIGHT

Poor nutrition, pre pregnancy weight and weight gain during pregnancy play a important role in causing preterm labour. Hickly and colleagues 2005 have low maternal prenatal gain is specifically associated with preterm birth.

4. STATURE

Short statured women have more tendencies to produce small babies

5. SOCIOECONOMIC STATUS

Women from lower socio economic status tends to be less educated and would not have satisfactory general, prenatal and antenatal care (Goffinet F 2005)

Universal effect of low socioeconomic status on health appears to directly affect the incidence of preterm labour (Moutquin, 2003)

6. ADDICTIONS

Women who smoke cigarettes or who abuse cocaine are at increased risk of preterm labour (Bens 2004) .Cigarette smoking has resulted in the increased incidence of pre term birth under 34 weeks gestation especially those who smoke more than 20 cigarettes per day. Smoking was initially implicated in the causation of placental abruption, placenta praevia and pre mature rupture of membranes but recent studies have proved strong association of smoking in pre term delivery. (Cnattingius 1998). Shah & Bracken reported that smoking was an important etiological factor in the causation of preterm delivery.Boer et al 1993, Volpe studied the increased incidence of pre term birth in women addicted to opiods.

There has been studies showing high incidence of preterm labour in women who abuse cochaine ,and it was partly attributed to the abruption caused by cochaine addiction.(B oer et al)

However there are not enough studies relating the risk of pre term labour with the consumption of alcohol.

7 Occupational hazards

Those involved in manual work are more prone for preterm labour

PREDISPOSING FACTORS

1. STRESS

Psychological factors such as depression, anxiety and chronic stress have been reported in association with preterm birth (Copper: 1996, Li 2008, Littleton 2007.Careers which involve considerable physical work and physical work and psychological stress are associated with increased preterm births (Papiernik and Kaninski 1994).Prolonged standing decreases the utero placental flow and increases the frequency of large placental infarcts causing growth retardation. Preterm birth is increased in women living alone, and those who are subjected to physical abuse. Henrikson et al 1995 reported that heavy vigorous exercise in the third trimester increased the risk of pre term delivery while regular and moderate exercise were actually showing a reduced risk.

2. COITUS

Yost NP et al in 2007 reported that coitus was not found to be associated but increasing numbers of sexual partners increased the risk of recurrent preterm delivery.

3. Reproductive history

a) Previous preterm birth

Spong, 2007 concluded prior preterm delivery to be a major risk factor for preterm labour.

History of one previous preterm birth is associated with a recurrence risk of 16-41 % (Williams 22nd edition) Risk increases with the number of preterm birth and decreases with the number of term deliveries.There is an increase in the risk of preterm delivery whenever there is a history of previous preterm delivery.This risk is on a increasing trend whenever the number of prior preterm births increases.(Hoffman 1981). When compared to a woman who has got a previous term delivery,women having a prior preterm delivery have threefold times the risk of reccurence.This risk becomes eight fold whenever there is a history of two preterm deliveries.Some of the integral factors that may contribute to the reccurence are the cervical length and inherent biological property of the cervix.

b) Previous abortion

There is increase in the preterm deliveries in women who experienced one or more second trimester abortions

c) Cervical incompetence

d) Uterine anomalies

e) Pregnancy complications

- ❖ Multiple pregnancies
- ❖ Hydramnios
- ❖ Preeclampsia
- ❖ Antepartum haemorrhage
- ❖ Second trimester bleeding not due to placental causes

4) **Interval between pregnancies**

Intervals shorter than 18 months and longer than 59 months associated with increased risk for preterm & small for gestational age infants (Conde – Agudelo 2006)

A significant increase in preterm births was observed when the interval between birth and LMP of next pregnancy was less than 3 months

Three fold increase in risk with a previous preterm compared to a previous term pregnancy (Bloom et al 2001)

A previous occurrence of preterm birth before 34 weeks may increase the risk of recurrence (Krymko et al 2004)

5**) Fetal Gender**

Fetal factor influencing the rate of preterm delivery is fetal sex, with preponderance of males delivering preterm.

MULTIPLE PREGNANCIES

Preterm delivery occurs in 43.6 percent of all term deliveries compared to 5.6 percent in singleton pregnancies (Patel et al 1983)

Monochorionicity has a greater association with preterm labour.

PREDICTION OF PRETERM LABOUR

RISK SCORING SYSTEM

Creasy and Govik had devised a risk scoring system for preterm labour. Women with scores of more than 10 or more are were considered to be at high risk for preterm labour.

Scoring systems are based on the factors which increase the risk of preterm delivery, the highest with a previous preterm delivery. Bleeding in pregnancy urinary tract infections, higher order pregnancies, body mass index < $20kg/m^2$ previous low birth weight babies and stress are associated with preterm delivery. Unfortunately risk scores don't identify the majority of women who deliver preterm .They are of limited clinical use (Honest H et al 2003)

Hueston 1995; Mercer 1996 studies failed to show any benefit from risk scoring systems.

As per ACOG 2008, Screening for risk of preterm labour other than risk factors is not beneficial in the general obstetric population. Owing to the low

predictive value of the risk factors, scoring systems have been identified to be of less value.However women presenting with some of the major clinical risk factors should be considered to be at risk of preterm delivery.

PAPIERNIK SCORING SYSTEM

Points	Socioeconomic factors	Previous Obstetric / Medical History	Social	Aspects of current Pregnancy
1	Two living children low socioeconomic status	H/o 1 abortion /less than 1 year of last child birth	Employed	Unusual fatigue
2	Maternal age <20 or >40 years /single parent	H/o 2 abortions	Smoker 10 Cigarettes / day/ moderate work	Gain <5g by 32 weeks
3	Very low socioeconomic status Ht < 150cm wt < 45 kg	H/o 3 abortion	Heavy work / long distance travelling	Breech 32 weeks / weight loss /head engaged at 32 weeks/febrile illness
4	Maternal age <18 years	Pyelonephritis		Bleeding after 12 weeks / short cervix open internal OS uterine irritability
5		Uterine anomaly second trimester abortion /DES exposure/cone biopsy		Placenta Praevia Hydramnios
6		Preterm delivery ,repeated second trimester abortion		Twins / abdominal surgical procedure

CERVICAL ASSESSMENT

CERVICAL DILATATION

Papiernik and colleagues (1987) in a study of cervical status before 37 weeks found that precocious cervical dilatation increased the risk of preterm labour. Levino and associates found that one fourth of the women who cervices were dilated 2 to 3 cm between 26 and 30 weeks delivered before 34 weeks Asymptomatic cervical dilatation after mid pregnancy has gained attention as a risk factor for preterm labour

Copper and associates 1995; Pereira and colleagues, 2007 verified cervical dilatation as a predictor of increased preterm delivery risk

CERVICAL LENGTH

I am and coworkers (1996) reported a mean cervical length at 24 weeks was approximately 35mm and those women with progressively shorter cervices experienced increased rates of preterm birth.

Owen associates (2001) reported a significant correlation of cervical length at 16 to 24 weeks and subsequent preterm birth before 35 weeks. They concluded in 2003 that the value of cervical length to predict birth before 35 weeks is apparent only in high risk preterm birth.

De Carvalho et al 2005 correlated sonographic cervical length, funneling and prior history of preterm birth with delivery before 35 weeks.

SONOGRAPHIC CERVICAL SCREENING

Transvaginal sonography allows an accurate assessment of cervix and is used to improve the accuracy of prediction of a woman going into preterm labour (Honest et al 2003) .Cervical length in a low risk population is normally distributed ,with a mean length at 23 weeks gestation of 35mm to 38 mm, the 10^{th} and 90^{th} percentile are approximately 25mm and 45mm respectively. The risk of preterm delivery is high if the cervical length was less than 25mm (Hassan et al 2000; To et al 2oo1)

Cook and associates (2000) showed that cervical length less than 21mm at less than 20 weeks gestation was associated with 95% delivery by 34 weeks gestation in women at high risk of preterm delivery.

Owen et al (2001) demonstrated that single TVS of cervix at 16 to 19 weeks with a cervical length of 25mm or less increased the risk of preterm delivery by 35 weeks gestation, 3.3 times.

Though there were studies including cervical funneling and dilatation for preterm labour risk parameters , cervical length was the main contributing factor

for the prediction of preterm delivery,and a cervical length of 25 mm was an important predictive factor.(To et al 2001)

Andrews et al (2000) found that fortnightly screening was found to be significantly helpful in prediction of preterm delivery.

CERVICAL INCOMPETENCE

Painless cervical dilatation in second trimester. It can follow prolapse and ballooning of membranes and ultimately expulsion of immature fetus.

CAUSES Previous cervical trauma – Dilatation and curettage

Conization

Cauterization

Albrechtsen and colleagues (2008) reported fourfold risk of pregnancy loss before 24 weeks.

FETAL FIBRONECTIN

Glycoprotein produced by a variety of cell types presents in high concentrations in maternal blood and amniotic fluid, placental tissue and the deciduas basalis. It is normally found in cevico vaginal secretions before 16 to 18 weeks gestation, before the fusion of fetal membranes and decidua is complete and also prior to onset of labour, but not normally present between 22 and 37 weeks gestation

Plays a role in intercellular adhesion during implantation and for maintenance of placental adhesion to uterine decidua (Lesson et al 1996)

Lockwood and co-workers (1991) reported that fibronectin in cervico vaginal secretions prior to membrane rupture were a possible marker for impending preterm labour.

Swabs are taken from the posterior fornix of vagina or the ecto cervix, ELISA with FDC 6 monoclonal antibody is used for the detection of fetal fibronectin .

Using ELISA technique, a value exceeding 50 ng/ml is considered positive. Quantitative tests take longer duration; therefore bed side tests have been developed in recent times to detect the presence and absence of fibronectin. However of concern is the high false positive rate if there is contamination with amniotic fluid, semen, and maternal blood and in patients with cerclage, rupture of membranes and pre eclampsia . Goldberg and coworkers 2000 reported, positive cervical or vaginal fetal fibronectin assay as a powerful predictor of preterm birth. The test is more accurate in predicting spontaneous preterm birth within 7 -10 days in women with symptoms of threatened preterm labour before cervical dilatation. Absence of fetal fibronectin carries a low risk in the occurrence of pre term births. But the utility of fetal fibronectin has been low in population with low risk

however combination of fetal fibronectin with clinical scoring has increased the positive prediction rate of pre term labour.

BIOCHEMICAL MARKERS

1) Salivary ostriol: progesterone ratio
2) Salivary oestriol > 1.8/ml before 34 weeks has sensitivity of 68% and specificity of 76% for preterm labour before 35 weeks of gestation(Darne et al)
3) Serum collagenase
4) Tissue inhibitor of metalloproteinase (TIMP)/Matrix metalloproteinases
5) Relaxin
6) Corticotrophin Releasing Hormone
7) Human chorionic gonadotrophin

These are of less practical value in prediction of preterm labour

Mediators of Inflammation And Infection

a. C – Reactive protein
b. Granulocyte elastase
c. Cytokines (IL-6, TNF)
d. Amniotic Fluid Glucose Concentration
e. Zinc

f. Lipocortin -1 (Romeo R et al)

g. Positive cultures

h. Granulocyte colony stimulating factor

These are not practically helpful in prediction of pre term labour

Fetal Breathing Movements

Absence of fetal breathing movements detected on ultra sound at the time of admission on women who presented with threatened pre term labour was found to be an accurate test in the prediction of spontaneous pre term labour.

Uterine Activity Monitoring

Although teaching a woman to self monitor her uterine contractions is a simple inexpensive method, there are lot of subjective variations in it which makes it less reliable .One of an earlier case control study reported a decrease in the preterm delivery rates on using the ambulatory monitoring system.(Katz et al 1986).

Currents opinion is that for most patients home uterine monitoring is no better than frequent nursing care and support. Only patients, who cannot recognize the presence of uterine contractions adequately like multi fetal gestation and over distended uterus may benefit from home monitoring.

DIAGNOSIS OF PRETERM LABOUR

Cunningham GH and coworkers (2001) found that preterm labour is established when regular uterine contractions occur at least 4 in 20 minutes or 8 in 60 minutes with progressive change in cervical score with effacement 80% or more and dilatation more than 1 cm contraction are 5 to 8 minutes apart.

Threatened preterm labour is a condition in which uterine contractions occur in the absence of cervical changes

SYMPTOMS

- Menstrual like cramps
- Low dull back ache
- Increase or change in vaginal discharge
- Uterine contractions 10 minutes apart or closer

4) Tococardiography

The amplitude, duration, shapes of contraction frequency and basal tone are monitored .The uterine activity is monitored.

Repetitive late decelerations, absent variability and variable decelerations are a sign of placental insufficiency.

PREVENTION OF PRE TERM LABOUR

Prevention is an important strategy in the management of a patient at high risk of preterm labour.

BASIC CARE

Development of family support, education, supportive services from health care providers

- Behavioral, life type modifications
- Cessation of smoking (Burguet et al)
- Adequate nutrition.
- Avoidance of illicit drugs

BED REST, HYDRATION AND SEDATION

Although bed rest and hydration are widely used as the first step of prevention, its practical benefit has been debatable. (Golden berg RL et al)

Kovacevich et al in his studies showed that bed rest of more than three days was associated with an increased occurrence of thrombo embolic events in women with threatened pre term labour.

Some studies have reported the increased risk of development of pulmonary edema, when intravenous fluids are administered during tocolytic therapy. There is no substantial evidence of hydration therapy in causing pregnancy prolongation. Hydration therapy however has been rarely studied as a single therapy in prevention or treatment of pre term labour.

Cochrane systematic review showed no significant difference in the risk of pre term labour in women who received hydration therapy.

Comparative trials have been conducted between combination of sedation with hydration vs intramuscular opiods in reducing the occurrence of preterm delivery and the results were found to be similar in both groups.

TREATMENT OF INFECTIONS

About 25 – 40 percent of preterm births are estimated to result from intrauterine infections (Cunningham et al 2010)

Morency and Buyold (2007) seemed to indicate that antibiotics given in the second trimester to women with a history of preterm labour would be effective in preventing recurrence of preterm labour

Most Randomized control trials show that intra vaginal clindamycin cream used to treat bacterial vaginosis did not preterm birth. Carey et al (2000) used oral metronidazole to treat bacterial vaginosis but did not find a reduction in preterm

birth. Systematic review concluded that screening and treatment of asymptomatic bacteruria and bacterial vaginosis may reduce the incidence of preterm in low risk population

CERVICAL ENCERCLAGE

Primary cerclages are placed prophylactically in women considered at high risk of preterm birth based on obstetric history

Secondary cerclages are placed when ultrasound findings are indicative of cervical insufficiency in high risk women

Tertiary cerclages are performed as an emergency procedure in the presence of positive clinical examination findings

The 1993 MRC/RCOG Multicenter Randomized trial concluded that clear benefit was seen only in patients with a history of three or more spontaneous births or preterm deliveries (Mac Naughton et al 1993)

In 2001, CIPRACT Trial, Cervical Incompetence Prevention Randomised Cerclage Trial showed that patients with cervical insufficiency and cerclage placement had a lower incidence of preterm delivery prior to 34 weeks (ALTHUISIUS ET AL 2001)

Rest et al 2000 concluded that cerclage failed to alter any perinatal outcome Daskalakis et al (2006) reported the benefits of emergency cerclage. In preterm

labour Dor et al 1982 and Roman et al 2005 reported that elective cerclage had no benefit in twin gestation . Two randomized trials by Lazar et al and Rush et al showed no benefit of routine cerclage in women at moderate risk for preterm labour.

PROGESTERONE

Progesterone given as weekly intramuscular injections of 17 α hydroxyl progesterone caproate from 16-20 weeks to 37 weeks showed significant reduction in preterm labour (Meis et al 2003) .It is not beneficial in twin pregnancies (Rouse et al 2007) (.Fonseca et al 2007) Micronized progesterone for asymptomatic women with very short cervix (less than 15mm) appear to be effective for prevention of preterm delivery.

As per ACOG (2008) progesterone is not recommended as a supplementary treatment to cervical cerclage for suspected cervical insufficiency or .as a preventive agent for asymptomatic women with a positive fetal fibronectin screen result or as a tocolytic agent. The role of progesterone in threatened preterm labour is uncertain. (Cochrane Systematic Review 2006)

MANAGEMENT OF PRETERM LABOUR

ROLE OF CORTICOSTEROIDS

In 1995 National Institute of Health consensus Development Panel recommended corticosteroids for fetal lung maturation in preterm infants. antenatal corticosteroids are recommended for all pregnant women between 25 and 34 weeks who are at risk of preterm delivery within 7 days

Cochrane systematic analysis reported that antenatal corticosteroids reduce neonatal death respiratory distress syndrome, intra ventricular hemorrhage, necrotizing enter colitis in first 48 hours of life as well as reduction in the need for intensive care monitoring & respiratory support later.

Though the maximum benefit of corticosteroid administration is between 24 hours and 7 days after initiation of therapy they provide surgical advantage even when baby is delivered within 24 hours.

Roberts and Dalziel (2006) reviewed antenatal corticosteroids for accelerating fetal lung maturity Bruschettini and colleagues (2006) studied equivalent of 12 mg versus 6 mg beta methadone and reported that the lower dose had less severe effects on somatic growth without affecting cell proliferation Eli main and co workers (2007) reported that beta methasone and dexamethasone were comparable in reducing the rates of major neonatal mortalities in preterm infants

TOCOLYTIC AGENTS

Tocolysis is pharmacological suppression of uterine activity.

Tocolytic drugs have been used in an attempt to inhibit preterm labour. They are effective in reducing the likelihood of delivery within 48 hours but do not reduce the overall risk of preterm labour. (ACOG 2007)

Tocolytics may be required

1. To gain 48 hours to administer antenatal steroids for increasing pulmonary maturity
2. To permit in utero transfer of the patient to a tertiary care centre for Multidisciplinary management
3. Prepare for neonatal care
4. Preparing the patient for an operative delivery

Variety of drugs which act on uterine smooth muscle to interrupt contractions are available these include magnesium sulphate, calcium channel blockers, oxytocin antagonists, Non steroidal anti inflammatory drugs (NSAIDS) and beta mimetic agonists

As per ACOG 2003, choice of tocolytic agent is individualized and is usually based on the maternal condition.

β SYMPATHOMIMETICS

Cartis et al noted that small dose of epinephrine inhibited uterine hyperactivity .Efforts to produce an epinephrine like compound which lacked the cardiovascular stimulant effect culminated in the synthesis of beta agonists

They react with β adrenergic receptors to reduce intracellular ionized calcium levels and prevent activation of myometrial contractile proteins Beta mimetics can cause mild fall in diastolic blood pressure and is used cautiously in patients of ante partum hemorrhage. they also cause a slight increase of blood sugar in non diabetic patient and hence can cause gestational diabetes when used for a longer duration alter thyroid function, elevated trans aminases hypo calcemia, anti diuresis and hypo kalemia are the other metabolic effects of beta mimetics.

Some of the neonatal side effects of beta mimetics include increased risk of hypo calcemia, hypo glycemia and intraventricular haemorrhage.

In recent time better drugs have replaced beta mimetics in regard to tocolytic function due to better profile of safety and less of adverse effects.

Classification

1st generation: Isoxsuprine, Orciprenaline, Isoprenaline,

2nd generation : Ritodrine, Terbutaline, Fenoterol

The most common used beta 2 agonist for tocolysis is ritodrine; then is terbutaline and salbutamol.

RITODRINE:

- Merkatz and colleages 1980 achieved a gestational age of 36 weeks in patients treated with ritodrine for threatened preterm labour.
- It is given as infusion at a dose of 50 μg/**min** and increased every 20 minutes until uterus is quiescent or side effects limit escalation of dose.
- However the drugs have been implicated as a cause of increased capillary permeability, disturbance of cardiac rhythm and myocardial ischemia.
- Side effects are palpitations, tremor, nausea, headache, chest pain dyspnea, pulmonary edema, hypokalemia, myocardial ischemia and arrhythmias.
- Ritodrine was withdrawn voluntarily in 2003, according to Federal Register, United States owing to its adverse effects

TERBUTALINE

- Not used as much as ritodrine, but is effective in temporary suppression of uterine contractions when given parenterally.
- Intravenous dose 5-10 μg/min ,increased every 10-15 min to a maximum of 80 μg. 2.5 – 5 mg is the oral dose given every 4-6 hours and 250μg subcutaneously every 20-30 minutes given as 4-6 doses.

- Terbutaline causes more hyperglycemia than ritodrine

Like ritodrine it can cause pulmonary edema (Angel and associates 1988) Gunin and associates (1998) reported no significant prolongation or improved neonatal outcome with terbutaline is not approved by the FDA and therefore its not mentioned in any protocol for pre term labour.

B2 agonists are no longer the first choice of drugs because of their side effects (RCOG 2002, Anotayanoth et al 2004)

Contraindications of beta 2 agonist :symptomatic cardiac disease, conduction disturbance, hyperthyroidism, sickle cell disease, uncontrolled diabetes mellitus, chorioamionitis, severe preeclampsia, multifetal gestation and severe obstetrical bleeding

Prostaglandin Inhibitors

Acetylsalicylate (Aspirin), Indomethacin naproxen fenamate, sulindac inhibit prostaglandin syntheses enzyme responsible for the conversion of free arachidonic acid to prostaglandins thereby decrease the myometrial gap junctions and influx of calcium.

Indomethacin was first used as a tocolytic by Zuckerman and associates (1974) various trials compared indomethacin with other drugs like ritodrine; Magnesium sulfate and found no difference in efficacy (Morales and coworkers (1989, 1193a)

Indomethacin is administered orally or rectally. A dose of 50 to 100 mg at 5 hours intervals, not to exceed 200 mg in 24 hours period.

Adverse effects reported are oligohydramnios, pulmonary hypertension due to constriction of ductus arteriosus. Intra cellular hemorrhage, necrotizing enterocolitis have also been reported.

Two randomized trials which compared the effect of indomethacin and placebo in delaying delivery showed no significant delay at 48 hours and 7 – 10 days.

Magnesium sulphate

Ionic magnesium in a sufficiently high concentration can alter myometrial contractility. Its role is presumably that of a calcium antagonist causing less intracellular calcium (Ca2+) to participate in actins myosin interaction during smooth muscle contraction.

Elliott in his study found that Magnesium sulphate was effective tocolytic in 87% cases.

Cox and associates in their study did not report any differences in the pregnancy outcome using magnesium sulphate.

It affects neural transmission by modifying acetyl chloline release and sensitivity of motor end plate.

Drug concentration and effect

- ❖ Contractility is inhibited at serum level of 5 – 8 mEq/L.
- ❖ Deep tension reflexes are lost at 9 – 13 mEq/L.
- ❖ Respiratory depression occurs at > 14 Meq/ dl

Loading dose of 4g IV given over 20 minutes followed by maintenance dose of 1 – 2 g / hour.

Side effect is nausea, giddiness, flushing, hypocalcaemia, respiratory depression, pulmonary edema and depressed motor respiratory activity in fetus.

Contraindications of magnesium sulfate are myasthenia gravis, heart block, renal disease and recent myocardial infarction

Neuro protective effect of magnesium sulfate was evaluated in (BEAM study-Beneficial Effects of Antenatal Magnesium Sulfate)

According to Gowther et al 2002, Cochrane systematic review, magnesium sulfate is an ineffective tocolytic.

Wilkens et al 1989 reported the occurrence of significant side effect of magnesium sulphate while being used concurrently with beta mimetics for tocolysis .

CALCIUM CHANNEL BLOCKERS

These agents act by reducing the influx of calcium ions into the cell membrane during the inward calcium current of action potential. They block the

voltage sensitive L type of calcium channels. They also decrease the tone of smooth muscles by inhibition of intracellular calcium from sarcoplasmic reticulum .Nifedipine is the most commonly used calcium channel blocker.

King and colleagues 2003, Papatson's 1997 concluded than calcium channel blockers especially **Nifedipine** are safer and more effective tocolytic agents than are beta agonists and have lower neonatal morbidity No significant change in utero placental flow has been reported .Mari et al (1989)

TREATMENT REGIMEN

Optimal dose regimen of Nifedipine has not yet been defined

George et al 1991, Read and Wellby (1986), showed that initial dose of 30 mg followed by 20 mg 8th hourly for 3 days had a success rate of 75% Andrenne et al gave a dosing regimen of 30 mg oral followed by a maintenance dose of 10 – 20 mg orally every 4 – 6 hours.

Most trials advocated an initial loading dose of 30 mg of oral Nifedipine followed by 10 to 20 mg every 6 hours. Sublingual Nifedipine is no longer advocated due to risk of sudden hypotension. Onset of action is less than 20 minutes with peak plasma concentration within 15 – 90 minutes.

Having a half life of 1.5 to 3 days. Elimination is mainly through kidneys (70%) and bowel 30%. Though the duration of action of a single dose can be as

long as 6 hours, there is no apparent cumulative effect when administered every 6 hours.

Side effects include facial flushing, nausea vomiting, headache, hypotension and tachycardia. No significant alteration in blood glucose and serum electrolytes was reported.

OXYTOCIN ANTAGONIST (ATOSIBAN)

Nonapeptide oxytocin analog is a competitive antagonist of oxytocin induced contractions.

Dosage: Recommended dose and administration schedule is a three step procedure. The initial bolus dose is 6.75 mg given over one minute, followed by an infusion of 18 mg/hour for three hours and 6 mg/hour for up to 45 hours. Treatment should not last longer than 48 hours and total dose given should not exceed 330 mg (RCOG, clinical Guidelines 2002)

Side effects include nausea, vomiting, chest pain, and dyspnoea

In randomized clinical trials, artesian failed to improve relevant neonatal outcome and was linked with significant neonatal morbidity (Moutquin and coworkers, 2000 Romero and associates 2000)

However, RCOG clinical guidelines 2002 suggested the first choice on administration of tocolytics to be oxytocin antagonist or Nifedipine.

NITRIC OXIDE DONORS (GLYCERYL TRINTRATE)

It is a potent endogenous hormone having smooth muscle relaxant property. Main action affects vasculature, gut and uterus.

NO donors act by inhibiting CRH (Corticotrophin releasing hormone, a promoter of parturition.

Dosage 10 mg Glycerol Tri nitrate patch placed over fundal region of maternal abdomen. Dose can be repeated with another 10 mg after one hour, if tocolysis is not achieved, to a maximum dose of 20 mg in 24 hours

Maternal hypotension is a common side effect.

In randomized clinical trials, Nitro glycerin administered orally, trans dermal or intravenously was not effective and was no superior to other tocolytics (Bistis 2004, Clavin 1996, Rees 1999, Buhimschi 2002. Duckitt K et al reported that nitroglycerine did not improve neonatal outcome or delay delivery on comparison with placebo, no treatment or alternative tocolytics.

POTASSIUM CHANNEL OPENERS

Diazoxide is related to thiazide diuretics and its main use is in the treatment of malignant hypertension. Its mechanism of action is inhibition of smooth muscle contractility, thereby causing uterine quiescence.

It is given in a dose of 5mg / kg, slow intravenous over 20-30 minutes. The drug is given after diluting with saline. Bolus dosage includes 50 -100 mg given every 5 minutes.

Side effects are tachycardia,

hyperglycaemia, decreased blood pressure, and decreased utero placental flow secondary to hypotension in the mother. Hypoglycaemia and fetal distress are the side effects which occur secondary to maternal hypotension.

AIM OF THE STUDY

1. To evaluate the Tocolytic effects of Calcium channel blocker – NIFEDIPINE in preterm labour
2. To study the maternal and fetal effects of NIFEDIPINE.
3. To compare the efficacy of Nifedipine with control group in delaying delivery for 48 hours in idiopathic spontaneous preterm labour

MATERIALS AND METHODS

STUDY DESIGN

It is prospective study conducted in Government RSRM Lying in Hospital, Stanley Medical College, and Chennai, from September 2012 to September 2013 The study population comprised of patients who attended the causality or outpatient department. There were 100 patients in Nifedipine group and 2 patients were lost to follow-up. There were 100 patients in Control group and 3 patients were lost to follow up. Study group received Nifedipine and control group were observed with bed rest. Both groups received intra muscular corticosteroids. Written informed consent obtained.

INCLUSION CRITERIA

1. Gestational age between 28 and 34 as determined by menstrual dates, clinical examination, and ultra sonogram
2. Uterine contractions 4 contractions in 20 minute period lasting for 40 – 45 seconds.
3. Cervical effacement of 75%
4. Cervical dilatation < 3 cm
5. Intact membranes.
6.

EXCLUSION CRITERIA

Maternal Conditions

- GA > 34 Weeks
- Rupture of membranes
- Evidence of chorioamnionitis
- Cervical dilatation greater than 4cm
- Ante partum hemorrhage
- Polyhyramnios / oligohydramnios
- Pregnancy induced hypertension
- Chronic hypertension
- Previous caesarean section
- Cardiac disease
- Renal disease
- Uncontrolled diabetes mellitus
- Asthma, Adult Respiratory distress Syndrome
- History of allergy
- Liver disease

FETAL CONDITION

- Multiple gestations
- Fetal death / distress
- IUGR
- Congenital anomalies

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INVESTIGATIONS

- Urine analysis
- Complete blood count
- High vaginal swab
- USG Abdomen
- ECG (Electrocardiogram)

DRUG PROTOCOL

On admission, patients were put in left lateral position. Temperature, pulse rate and blood pressure recorded .Cardiovascular system and Respiratory system examined.

GROUP A

Tab. Nifedipine 20 mg was given orally. If uterine contractions persisted after 90 minutes another 10 mg dose given. If the dosage suppressed uterine activity then maintenance of 10 mg given 6^{th} hourly for 3 days. Dosage is gradually tapered and stopped.

If uterine contractions did not cease within 1-1/2 hours patient was deemed failure and treatment stopped .Treatment considered success if there was abolition of uterine contractions and progress of cervical dilatation and postponement of labour for at least 48 hours.

GROUP B

- Patients observed with bed rest
- Both the groups given intramuscular corticosteroids

- Monitoring of vitals – Temperature, Pulse rate
- Blood pressure Respiratory rate

- Systolic BP<100 mm Hg or pulse rate > 100,
- Temperature > 37.5°C is important

- Careful watch for side effects like facial flushing ,tachycardia, hypertension, nausea and vomiting

After initial reactive CTG (Cardio tocography), fetal heart rate monitored hourly during stabilization phase and there after fourth hourly for first 48 hours

Success and Failure

There are several studies by various authors suggesting several factors for assessment of success of tocolysis.

In our study, successful tocolysis was defined as the delay of delivery with suppression of contractions for more than 48 hours from initiation of therapy.

Failure of therapy is said to occur, when patient delivered within 48 hours of initiation of therapy and tocolysis was stopped when cervical dilatation progressed to > 3 cm or when there was spontaneous rupture of membranes.

Hence our study is confined to idiopathic spontaneous preterm labour and comparing the efficacy of Nifedipine with that of control in delaying delivery for 48 hours and regarding the maternal and fetal effects of Nifedipine

RESULTS

AGE DISTRIBUTION

Table: 1

Age in years	Nifedipine group		Control group		Percentage
	No.	%	No.	%	%
<19	12	12.2%	16	16.4	14.36
20 – 24	34	34.6	43	44.3	39.4
25 – 29	43	43.8	31	31.9	38.14
>30	9	9.1	7	7.2	8.20

Maximum incidence of preterm labour occurred in age group 20 – 24 years being 39.4%.

Incidence of preterm labour in age group less than 19 years and more than 30 years was 22.5%

ANTENATAL REGISTRATION

Table: 2

Booked / Unbooked	Nifedipine group		Control group	
BOOKED	79	80.6%	84	86.5%
UNBOOKED	19	19.38%	13	13.4%

Incidences of preterm labour in booked and unbooked cases were 83.5%and 16.44 % respectively.

OBSTETRIC HISTORY

Table: 3

Gravida	Nifedipine group		Control group		Percentage
PRIMI	67	68.3%	62	63.9%	66.1%
PARA Iand above	31	31.6%	35	36%	33.8%

Incidence of preterm labour among primi gravida and multi gravida were 66.1% and 33.8% respectively.

GESTATIONAL AGE

Table: 4

GA weeks	Nifedipine group		Control group	percentage
28 – 30	30	30.6%	31	31.28%
31 – 34	68	69.38%	66	68.04%

Incidence of preterm labour between 28-30 weeks is 31.28 %and between 31-34 weeks is 68.o4%

SUCCESS OF TOCOLYSIS

Table: 5

Success/Failure	Nifedipine group		Control group	
SUCCESS	72	73.4%	32	32.9%
FAILURE	26	26.5%	65	67.01%

The success in Nifedipine and controls are 73.4% and 32.9% respectively. By test of proportion p value was found to be < 0.001 which is statistically significant.

DOSAGE REQUIRED

Table: 6

S NO	DOSE	NO.	%
1.	20mg	21	21.4%
2.	30mg	77	78.57%

78.57% of patients required 30 mg to suppress uterine contractions whereas 21.4% required 20 mg to suppress uterine contractions.

RESPONSE ACCORDING TO GESTATIONAL AGE

Table: 7

GA weeks	**Nifedipine group**				**Control group**			
	S		F		S		F	
	No	%	No	%	No	%	No	%
28 – 30	8	11.1%	22	84.6%	3	9.3%	35	53.84%
31 – 34	64	88.8%	4	15.38.%	29	90.6%	30	46.15%

Prolongation of pregnancy more than 48 hours is 88.8% and 90.6% in 31-34 weeks gestational group between nifedipine and control groups respectively. 9.3% and 11.1% in 28-30 weeks gestational group are in control and nifedipine groups respectively.

DURATION OF PROLONGATION

Table: 8

DURATION OF PROLONGATiON	Nifedipine group		Control group	
	No.	%	No.	%
<48 hours	26	26.5%	65	67.01%
48 hours	52	53.06%	32	32.9%
Upto 72 hrs	13	13.2%	0	
Upto 5 days	5	5.1%	0	
Upto 1 week	2	2.o4%		

Prolongation of delivery beyond 48 hours was seen in 53.06% in nifedipine group compared to 32.9% in control group. Delivery occurred within 48 hours in 26.5% in nifedipine group compared to 67.01% in control group

SIDE EFECTS OF NIFEDIPINE

Table: 9

1	Tachycardia	15
2	Headache	20
3	Hypotension	7
4	Nausea vomiting	10
5	Facial flushing	3

About 56.1% patients had side effects .Headache and maternal tachycardia was commoner among the side effects.

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FETAL MORBIDITY

Table: 10

	Nifedipine group		Control group		%
	S	F	S	F	
BIRTH ASPHYXIA	1	2	2	2	3.5%
Rds	2	4	4	11	10.7%
Sepsis	4	3	6	4	8.71%
IVH	1	1	1	2	2.5%

About 11.1 % and 38.46% of neonatal complications occurred in nifedipine success and failure groups respectively.

About 40.6% and 29.23 % of neonatal complications occurred in control success and failure groups.

NEONATAL MORTALITY

Table: 11

	Nifedipine group		**Control group**	
	S	F	S	F
	6	8	9	13

Neonatal mortality was 14.28 % and 22.8. % among Nifedipine and control groups respectively

OVERALL NEONATAL MORTALITY WAS 18.46% AMONG BOTH GROUPS.

APGAR SCORE

Table: 12

5' APGAR	Nifedipine group				Control group			
	S		F		S		F	
	No.	%	No.	%	No.	%	No.	%
≤ 5	3	4.1%	12	46.1%	8	25%	42	64.6%
6-7	16	22.2%	4	15.3%	6	18.75%	10	24.6%
>7/10	53	73.6%	10	38%	18	56.2%	4	10.7%

Among the success groups, 73.6% belonged to Nifedipine, 56.2% belonged to control group having apgar >7

P value <0.001 significant.

WEIGHT OF BABY OF BIRTH

Table: 13

BIRTH WEIGHT	Nifedipine group				Control group			
	S		F		S		F	
	No	%	No	%	No	%	No	%
<2	5	6.9%	24	92.3%	12	37.5%	39	60%
2-2.5	61	84.7%	2	7.69%	18	56.2%	26	40%
>2.5	6	8.3%	-	-	2	6.25.%	-	-

84.7% cases among Nifedipine success groups had birth weight of 2-2.5 kg when compare with 56.2% in control success group.

8.3% in Nifedipine success group had birth weight >2.5 kg compared to 6.25% in control success groups. p value 0.001 statistically significant.

RESPIRATORY DISTRESS SYNDROME

Table: 14

RDS	Nifedipine group				Control group			
	S		F		S		F	
	No.	%	No.	%	No.	%	No.	%
PRESENT	2	2.7%	4	15.38%	4	12.5%	11	16.9%
ABSENT	70	97.2%	22	84.61%	28	87.5%	55	84.6%

Incidence of RDS is 2.7% and 15.38% in nifedipine success and failure respectively, compared to 12.5% and 16.9% in control success and failure groups. P value 0.042.statistically significant

DISCUSSION

In our study the range of gestational age was 28 to 34 weeks. In other studies it was 24 to 32 weeks (Nikolov et al) and 26 to 34 weeks (Bekkari et al). In Cochrane meta analysis study, the inclusion range of gestational age was from 20 to 26 weeks upto a maximum of 36weeks. The mean gestational age in Systematic meta analysis review was 29.1 to 32.4 weeks. The trials in the Meta analysis excluded women with cervical dilatation more than 4cm, while in our study the limit was 3cm.

In our study the dosage of Nifedipine used as 20 mg of loading dose followed by 10 mg at 90 minutes, if uterine contraction persisted, followed by maintenance dose of 10 mg of oral nifedipine 6 hourly for 3days. Similar to this a loading dose of oral nifedipine 3x10mg was used by Bekkari et al A loading dose 4x10 mg of oral nifedipine was used by Nikolov et al in their study.

In Cochrane meta analyis the maximum dose used was 40 mg of oral nifedipine in the first hour followed by 20mg of slow release nifedipine at t=90 minutes (Papatsonis et al).

Most of the trials in the Cochrane meta analysis measured outcome primarily by delay in delivery for more than 48 hours as in our study. 9 out of 13 trials in this review reported a favorable outcome. Bekkari et al and Nikolov et al reported a success of 84% and 86.4% respectively, while in our study it was 73.4%

The most common side effects in the trials in Cochrane meta analysis were hypotension and headache similar to our study. Similar to our study there was no maternal mortality in any of those trials. No maternal side effects and good patient tolerance were reported by Nikolov et al and Bekkari et al respectively in their studies.

Similar to our study there was a reduction in respiratory distress syndrome and improved Apgar scores at 5 minutes in Cochrane meta analysis. According to Systematic Review and Metaanalysis on Efficacy and safety of nifedipine for management of preterm labour (2011) , maintenance tocolysis using nifedipine was ineffective in prolonging gestation or improving outcomes when compared with placebo or no treatment. Twenty six trials were included and it was concluded that nifedipine was associated with significant reduction in risk of delivery within 7 days of initiation of treatment. When compared with any other tocolytic agent (mainly beta mimetic).

SUMMARY

1. In our study, Preterm labour was common in Primigravida in age group 20 – 29 years accounting for 77.54% compared to 22.5% between 19 and 30 years.
2. Incidence of preterm labour in booked and unbooked cases were 80.6% and 19.38% in nifedipine group when compared to 86.5% and 13.4% in control groups respectively.
3. The success of Nifedipine as indicated by prolongation of pregnancy beyond 48 hours was observed in 73.4% of cases compared with 57% in controls P value was significant (< 0.001).
4. 78.57% of patients required 30 mg to suppress uterine contractions whereas 21.4% required 20 mg to stop contractions.
5. The prolongation of pregnancy more than 48 hours was found to be more in 31 -34 weeks of gestational age in Nifedipine and control groups.
6. Prolongation of pregnancy more than 48 hours was seen in 53.06% in nifedipine group compared to 32.9% in control group
7. Delivery occurred within 48 hours in 26.5%in nifedipine group compared to 67.01% in control group.
8. About 56.1% of patients in Nifedipine group had side effects which were reversed on discontinuation Headache ,maternal tachycardia were the common side effects

9. There was no maternal mortality
10 About 11.1% and 38.46% of neonatal complications occurred in nifedipine success and failure groups respectively.
11. About 34.37 % and 21.5% of neonatal complications occurred in control success and failure groups.
12. Neonatal mortality was 14.28% and 22.6% among Nifedipine and control groups respectively
13. Apgar score of ≤5 was seen in 4.12% and 46.1% of Nifedipine success and failure groups respectively.
14 Apgar 6-7 was seen in 22.2% and 15.3% of Nifedipine success and failure groups.
15. Apgar more than 7 was seen in 73.6% and 38% of Nifedipine success and failure groups.
16. 84.7% Cases among Nifedipine success group had birth weight of 2 to 2.5 kg when compared with 56.2% in control success group.
17. 8.3% in Nifedipine success group had birth weight > 2.5kg compared to 6.5% in control success group P value 0.001 statistically significant.
18. Incidence of Respiratory Distress syndrome is 2.7 % and 15.38% in Nifedipine success and Failure respectively compared to 12.5% and 16.9% in control success and failure groups P value

CONCLUSION

Labour inhibiting drugs may not treat the cause of preterm labour but they only treat the symptom that is contractions.

These agents make the uterus refractory to contractile stimuli for a short time so that the prenatal outcome is improved. In this clinical study idiopathic spontaneous preterm labour whose onset was at 28 to 34 weeks has responded well to tocolytic therapy by oral nifedipine and neonatal outcome improved and no maternal mortality was observed. The maternal side effects were reversed on discontinuation of the drug. The drug has provided the fetus of its valuable opportunity of being inside the mother's womb for a period enough to make the lungs mature by administration of exogenous steroids.

However decrease in the incidence of preterm labour lies in identification of high risk patients, improving the socio- economic standards, better antenatal care, education and early detection of the onset of labour.

In developing countries neonatal intensive care are usually found in tertiary referral hospitals but not all such units have the required treatment capabilities. The statistically significant benefits of nifedipine in suppressing the uterine contractions for in utero transfer, in reducing neonatal respiratory distress syndrome along with its reduced maternal side effects, and its low cost makes it to be considered as the first line tocolytic agents in these countries

BIBLIOGRAPHY

1. Adrienne Z, Able S, Ana Maria Romero, MD, Suneet P, Chauhan. Use of Calcium channel antagonist for preterm labour. Obstet Gynecol Clin NAM; 32 (2005) 519-525.
2. American College of Obstetricians and Gynecologists. Preterm labour. Technical bulletin no. 206. Washington, D.C: ACOG, 1995.
3. Amy E.Hearne, MD and David A. Nagey. Therapeutic agents in Preterm labour: Tocolytic agents. Clinical Obstetrics Gynaecology 2000; vol 43, Number 4, 787-801.
4. Anderson A, 1977, Preterm Labour – definition in Anderson A (ed) Proceedings of the fifth study group of the Royal college of Obst and Gynaecol. RCOG.
5. Baud O, Kaminski M, Audibert F, Jarreau PH, Paperniek E, Huon C, Leperc J, Dehan M, Lacaze T. Antenatal Glucocorticosteroid treatment and cystic periventricular leucomalacia in very premature infants. N Engl Med 1999 Oct 14;341 (16): 1190-6.
6. Baumgartens et al., perinatal medicine Vol.5, 1974.
7. Bekkari Y, Lucos J, Beillat T, Cheret A, Dreyfus M. Tocolysis with Nifedipine: its use in current practice. Gynecol Obstet Fertil. 2009 Dec;3 (12): 1054-5.

8. Bergmers I, et ao., Cause of hearing loss in the high risk premature infant J. Pediatr. 1985; 106: 95-101.
9. Berns S: Understanding Prematurity. Presentation at the 26th Annual International Neonatal Conference. Miami, FC, 2002.
10. Bobitt JR, Ledger WJ, Unrecognised amnionitis and Prematurity: A Report. J. Reprod. Med. 1977: 19:8.
11. Bobitt J.R., Damato J.D., Sakaini J. Perinatal complications in Group B streptococcal carriers: A longitudinal study of prenatal patients; Am. J. Obstet. Gyneco. 1985; 151:711.
12. Brayant Green wood G.D. Relaxin. Cambridge university press PP. 252- 264.
13. Burguet A, Kaminski M, Abraham Lerat L et al. Epipage Study group. The complex relationship between smoking in pregnancy and very preterm delivery. Results of the Epipage study Br J Obstet Gynaecol 2004; 111: 258-265.
14. Carret JC, Klebanoff MA, Hauth JC, Hillier SL, Thom EA, Ernest JM, et al. Metronidazole to prevent preterm delivery in pregnant women with asymptomatic bacterial vaginosis. National Institute of Child Health and Human Development Network of Maternal – Fetal medicine units. N. Engl J Med 2000 Feb 24, 342(8) 534-40 plan. 1979 vol 133 40-5.

15. Caritis stebe et al. Pharmacological inhibition of preterm labour Am J. OG plan. 1979 vol. 133 40-5.
16. Change C. Smith R. Sterinhoff P. et al. Induced abortion and spontaneous fetal loss in subsequent pregnancies Am. J. Public Health 1982; 72:548.
17. Cox SM, Sherman ML, Leveno KJ. Randomised investigation of magnesium sulfate for prevention of preterm birth. Am J. Obstet Gyneol 199; 163: 767-72.
18. Cox SM, King MR, Casey ML, et al: Interleukin – 1 beta, - 1 alpha and – 6 and prostaglandins in vaginal / cervical fluids of pregnant women before and during labour. J Clin Endocrinol Metab 77: 805, 1993.
19. Crowther CA, Hiller JE, Doyle LW. Magnesium sulfate for preventing preterm birth in threatened preterm labour. Cochrane Database Syst Rev 2002: Issue 4: CD 1001060.
20. Cunnigham GH, Gant NF, Leveno KJ. Preterm birth in: Williams Obstetrics. 21st ed. Mc Graw Hill. USA. 2001; 27: 689-728.
21. Da Fonseca EB, Bittar RE, Carvalho MHB, et al: Prophylactic administration of progesterone by vaginal suppository to reduce the incidence of spontaneous preterm birth in women at increased risk. A Randomised placebo-controlled double blinded study. Am J Obstet Gynecoll 188: 419, 2003.

22. Daskalakis G, Papapanagiotou A, Mesogitis S. Bacterial vaginosis and Group B streptococcal infection and preterm delivery in low risk population. Fetal Diagn Ther 2006; 21(2): 172-6.
23. Darne J. eet al., increased salivary oestriol to progesterone ratio before preterm delivery: Possible predictions for preterm labour Br. Med. J 1987: 294-270-272.
24. Drilhen C.M. The social and economic factors affecting the incidence of premature birth. J. Obstet. Gynaecol. Br. Emp. 1957; 64: 161-184.
25. Duckitt K, Thorntons. Nitric Oxide donors for the treatment of preterm labour. The Cochrane Database of Systematic Reviews 2002, Issue 3. Art No. CD002860.
26. Edwards L.E Barrada M.L., Hamann A.A et al., Gonorrhoea in pregnancy Am. J. Obest Gynecol 1978; 132:637.
27. Ferguson JE, Dyson DC, Schutz T, Stevenson DK, A comparison of tocolysis with nifedipine and ritodrine. Analysis of efficacy and maternal fetal and neonatal outcome. Am. J. Obstet Gynaecol 1990: 163: 105-11.
28. Fernando Arias, Shirish N Daftary, Amarnath G Bhinde. Practical guide to high risk pregnancy and delivery; 3rd edition, page 203.

29. Freda MC, De Vore N, Should intravenous hydration be the first line of defense with threatened preterm labour? A critical review of the literature. J Perinatol 1996 Sep-Oct; 16(5): 385-9.

30. Gravett MG, Hummel D, Eshenbach DA. Et al., Preterm labour associated with subclinical amniotic fliud infection and with bacterial vaginosis.

31. Foffinet F, Primary predictors of preterm labour BIOG 2005 mar; 112 Suppl 1:

32. Goldenberg RL. The management of preterm labour Obstt Gynecol 2002: 100(5): 1020-37.

33. Goldenberg R and Rouse D. Prevention of premature birth. N Engl J ked 1998; 339: 313-20.

Gonik B, Greasy R.K. Pretem labour. Its diagnosis and management Am. J. Obs & Gyn. 1986; 154: 3-8.

34. Graham M. el al., Production of cerebral palsy in very low birth weight infant. Prospective ultrasound study Lancet 1987; 2: 593-596.

35. Harison R.F. Hurley R, Dehouvois J., Genital Mycoplasma and birth weight in offspring of primigravida women. Am. J. Obstet. Gynecol. 1979; 133:20.

36. Harison H.R., Alexander E.R., Weinstein L., et al Cervical Chlamydia trachomatis and Mycoplasmal infections in pregnancy. Epidemiology and outcome JAMA 1983; 250:1721.

37. Honest H. Bachmann LM, Coomarasamy A, Gupta JK, Kleijnen J, Khan KS. Accuracy of cervical trans vaginal sonography in predicting preterm birth a systematic review, Ultrasound obstet Gynecol 2003; 22: 305-322.
38. Honest H, Bachmann LM, Gupta JK, Kleijnen J, Khan KS. Accuracy of cervicovaginal fibronectin test in predicting results of spontaneous preterm birth: systematic review BMJ 2002; 325:301.
39. Honest H, Bachmann LM, Sundaram R, Gupta JK, Kleijnen J, Khan KL. The accuracy of risk scores in predicting preterm birth – a systematic review. J Obstet Gynaecol 2004; 24: 343-359.
40. Ian Donalds Practical obstetric problems. Preterm birth; 6th ed; pg 395.
41. Katz M, Newmann RB, Gill PJ. Assesment of uterine activity in ambulatory patients at high risk of preterm labour. Am J Obste Gynecol. 9186; 15: 44-47.
42. Kekki M, Kurki T, Pel Konen J, Karkihen – Raty M, Cacciatore B, Poaavonen J. Vaginal Clindamycin in prevention preterm birth and peripartum infections in asymptomatic women with bacterial vaginosis: a randomized control trial Obstet Gynecol 2001 May; 75(5 pt 1): 643-8.
43. Klein H, Keirse KJNC. How accurate is a womans diagnosis of threatened preterm delivery. Br. J. Obstet. Gynecol 1991; 97:317.
44. Klein LC, Gibbs RS. Infection and Preterm Birth. Obstet Gynecol Clin North Am 2005 Sep; 32(3): 397-410.

45. King JF, Flenady V, Papatsopnis D, Dekker G, Carbonne B. Calcium Channel blockers for inhibiting preterm labour. Cochrane Database of Systematic Reviews 2003, Issue 1. Art. No. CD002255.

46. King JF, Flenady V, Papatsonis D, Dekker G, Carbonne B. Calcium Channel blockers for inhibiting preterm labour; a systematic review of the evidence and a protocol for administration of Nifedipine. Aus NZ J Obstet Gynecol 2003; 43: 192-198.

47. Lamont R. F Taylor – Robinson D Newman K et al., Spontaneous early preterm labour associated which abnormal genitial bacterial colonization. Br. J. Obstet. Gynaecol 1986; 93:804.

48. Lazar P., Guegen S, Dreyfus J. et al. Multicentered controlled trial of cervical cerclage in women at moderate risk of preterm delivery, Br. J. Obstet. Gynecol. 1984; 91:731.

49. Levit EM, Baker LS, Corman H, et al: The direct cost of low birth weight. Future child 5.35, 1995.

Leitich H. Controversies in diagnosis of Preterm labour. Br J Obstet Gynaecol 2005 Mar, 112. Suppl 1:61-3.

50. Lock wood C.J. et al., Fetal fibronection in cervical and vaginal secretion as a predictor of preterm delivery. Engl J. Ned. 1991: 325: 669-674.

51. Lumley J.M, Lieberman E. Ryan K.J. et al., Interpregnancy interval and risk of preterm labour. Am. J. of epidemiology 1993: 122; 304-309.
52. Luke B, Mamelle N, Kerth L, et al: The association between occupational factors and preterm birth: A United States nurses study. Am J Obstet Gynecol 173: 849, 1995.
53. MacGregor S. N, Keith L.G., Chasnoff I.J., Cocaine using pregnancy: Adverse perinatal outcome. Am. J. Obstet. Gynecol. 1987; 157:686.
54. Meis PJ, Goldenberg RL, Mercer BM, et al. The preterm prediction study: Risk factors for indicated preterm births. Am J Obstet Gynecol 178:562, 1998.
55. Meis PJ, Michielutte R, Peters TJ, etal: Factors associated with preterm birth in Cardiff, Wales. Univariable and multi-variable analysis. Am J Obstet Gynecol 173:590, 1995b.
56. Meis PJ. National Institute of Child Heealth and Human Development Maternal Fetal Medicine Units Network. 17 alpha – hydroxyl progesterone acetate to prevent recurrent preterm biorth. Am J Obstet Gynecol 2002; 187;
57. Meis PJ, Klebanoff M, Thorn E etal. National Institute of Child Health and Human Development Maternal – Fetal Medicine units network. Prevention of recurrent preterm delivery by alpha – bydroxy progesterone caproate. N Engl J med 2003; 348: 2379-2385.

58. Meyer M.B., Jonas B.S., Tonsascia J.A.Perinatal events associated with maternal smoking during pregnancy. Am. J. Epidemiol. 1976; 103; 464.

59. Morrison et al: Fibronectin a predictor of preterm delivery. Br. J. Obs. And Gyn. 1993; 100:969.

60. MRC/RCOG working party on cervical cerclage, final report of the Medical Research Council/Royal College of Obstetricians and Gynecologists. Multicentre randomized trial of cervical cerclage. Br J Obstet Gynaecol 1993; 100: 516-523.

61. Nikolov A, Markov D, Dimitrov A, Ivanov S, Diavolov V. Treatment of preterm delivery with Calcium channel blockers. Nifedipine. Akush Ginecol (sofia). 2007; 46(9): 18-22.

62. Owen J, Iams JD, Hauth JC: Vaginal Sonography and cervical incompetence. Am J Obstet Gynecol 188: 586, 2003.

63. Papatsonis DNM, Vangujn HP, des HJ Lange FM, Bleker OP, Dekkar GA Nifedipine and ritodrine in Management of preterm labour. A randomized multicenter trial. Obstet. Gynaecol 1997; 90: 230-4.

64. Papatsonis D, Flenady V, Cole S, Locey H. Oxytocin receptor antagonists for inhibiting preterm labour. Cochrane Database Rev 2005; (3): CD 004452.

65. Papiernik E. et al., precocious cervical ripening and preterm labour. J Obst and Gyn. 1987; 162: 1150-1153.

66. Read MD, Wellby DE. The use of calcium channel antagonist (Nifedipine) to suppress preterm labour. Br. J. Obstet Gynecol. 1986; 93: 933-7.

67. Reiss et al. Role of indomethacin in preterm labour. Int. J. Obstet Gynecol. 1976, 143, 369-374.

68. Richey SD, Ramin KS, Roberts SW, Ranain SM, Cox-SM, Twickler DM; The correlation between transperineal sonography and digital examination in the evaluation of third trimester cervix. Obstet. Gynaecol 1995; 85:745.

69. Roberts D, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database of Systematic Reviews 2006, Issue 23. Art. No. CD004454.

70. Robertson J.G., Livingstone J.R.B., Isdale M.H., The management and complications of asymptomatic bacteruria in pregnancy. Br. J. Obstet. Gynaecol. 1968:78:59.

71. Romeo R. Sepulveda W. Lipocortin 1 in term and preterm parturition, Chicago Proceedings of society for gynecologic investigation 1993; 217.

72. Royal College of Obstetricians and Gynecologists Guideline: Tocolytic Drugs for Women in Preterm Labour 1 (B) London: RCOG, 2002.

73. Rush R.W, Keirse M.N. M.C. et al, Contribution of preterm delivery to perinatal mortality Br. Med. J. 1976: 965-968.

74. Sexually Transmitted Diseases. Treatment Guidelines. 2002. MMWR. Centers for disease prevention and Control.

75. Tocolytic drugs for woman in preterm labour. RCOG clinical guideline NBo. (B) October 2002.

76. Varma R, Gupta JK. Antibiotic treatment of bacterial vaginosis in pregnancy; multiple metaanalysis and dilemmas in interpretation. Eur J. Obstet Gynecol Reprod Biol 2006 Jan 1; 124(1): 10-4.

77. Varner M. W. et al., Amniotic fluid zinc level during term labour, preterm labour and Chorioamnionitis. Chicago, Proceeding of Society for gynaecologic investigation 1994-401.

78. Varner MW, Esplin MS. Current understanding of genetic factors in preterm birth. Br J Obstet Gynaecol 2005 Mar; 112 suppl 1: 28-31.

79. WHO 1977. Manual of international classification of diseases, injuries and causes of death Vol. I WHO Geneva.

80. Williams Obstetrics 22nd ed, Chapter 36, Preterm birth; pg 859.

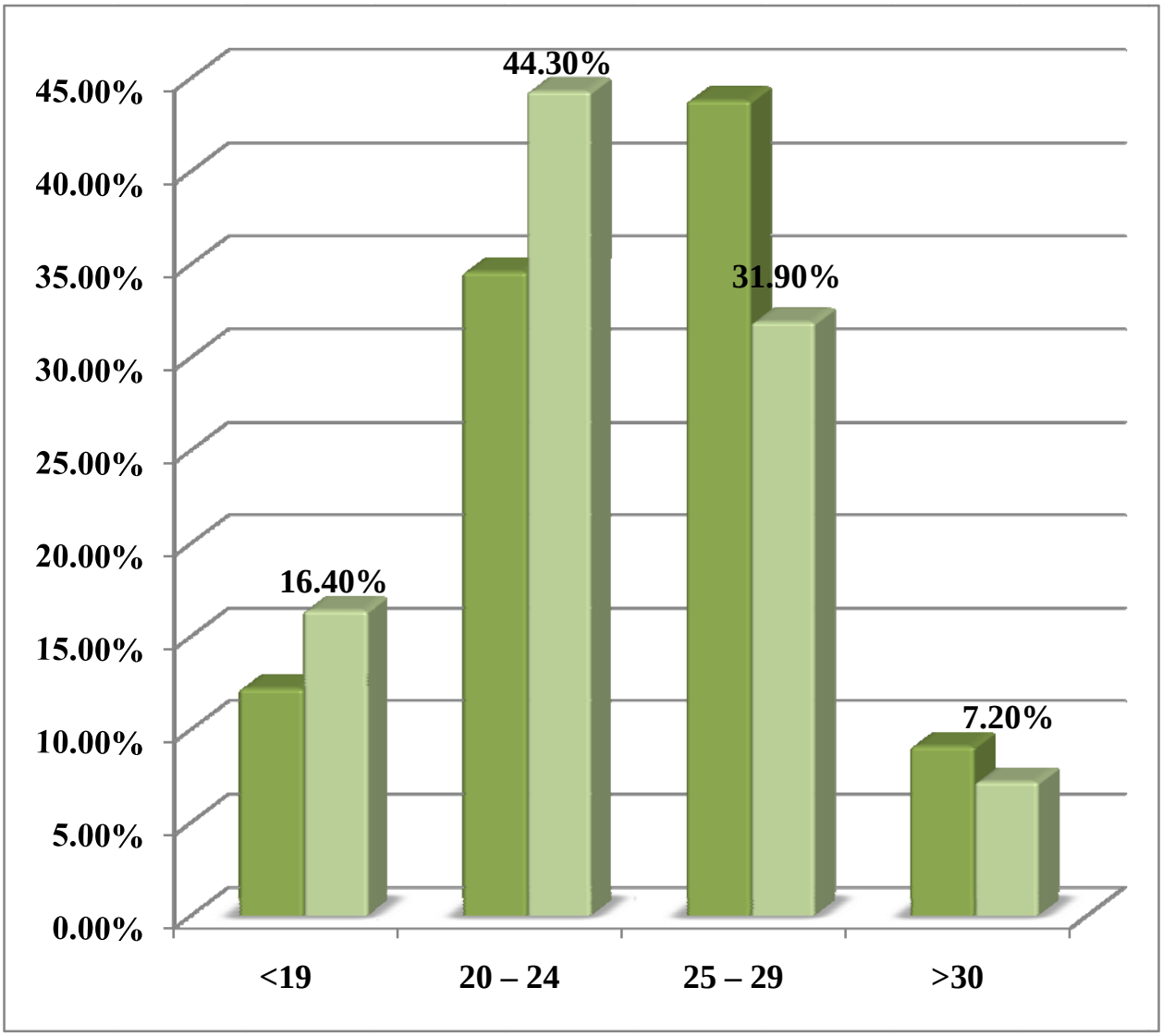
81. Worldwide atosiban versus beta agonists study group: Effectiveness and safety of the oxytocin antagonist atosiban versus beta adrenergic agonists in the treatment of preterm labour. The worldwide atosiban versus beta – agonist study group Br. J Obstet Gynecol 2001 Feb: 180(2): 133-42.

82. Xiong X, Buekens P, Fraser WD. Periodontal disease and adverse pregnancy outcomes: a systematic review. Br J Obstet Gynaecol 2006 Feb; 113(2): 135-43.

83. Yost NP, Owen J, Berghella V. Effect of coitus on recurrent preterm birth. Obstet Gynecol 2006 Apr 107 (4): 793-7.

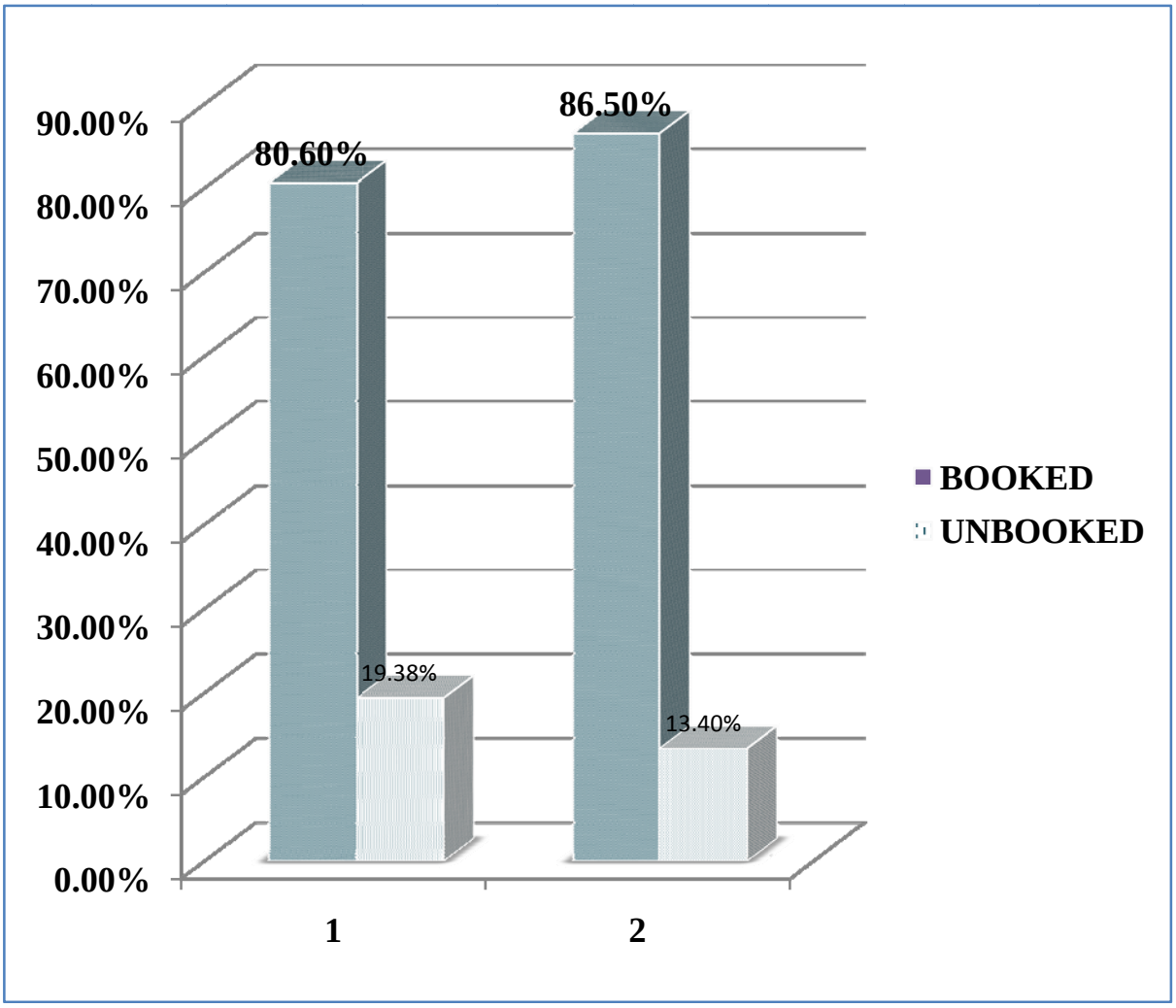
AGE DISTRIBUTION

Table: 1



ANTENATAL REGISTRATION

Table: 2

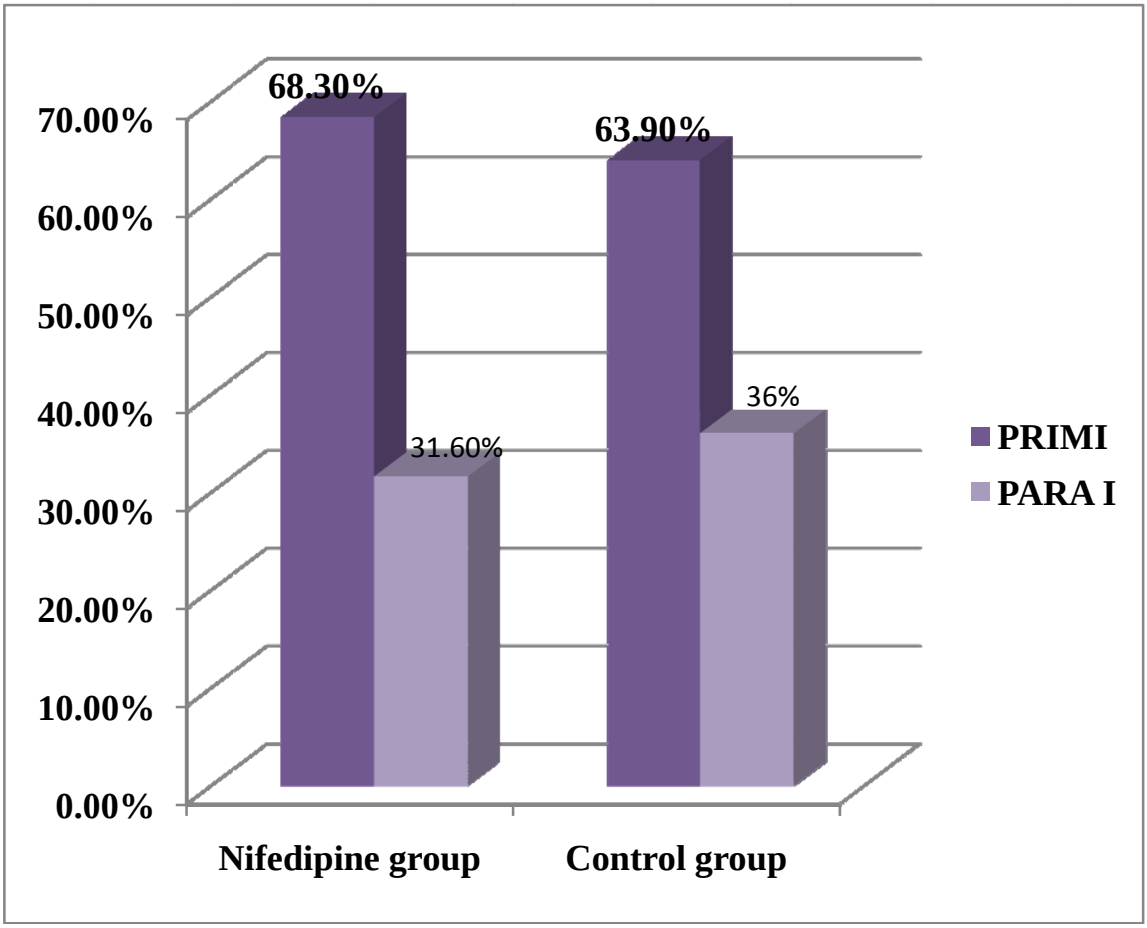


1- Nifedipine group 2- Control group

Incidence of preterm labour in booked and unbooked cases were 83.5 and 16.44 % respectively.

OBSTETRIC HISTORY

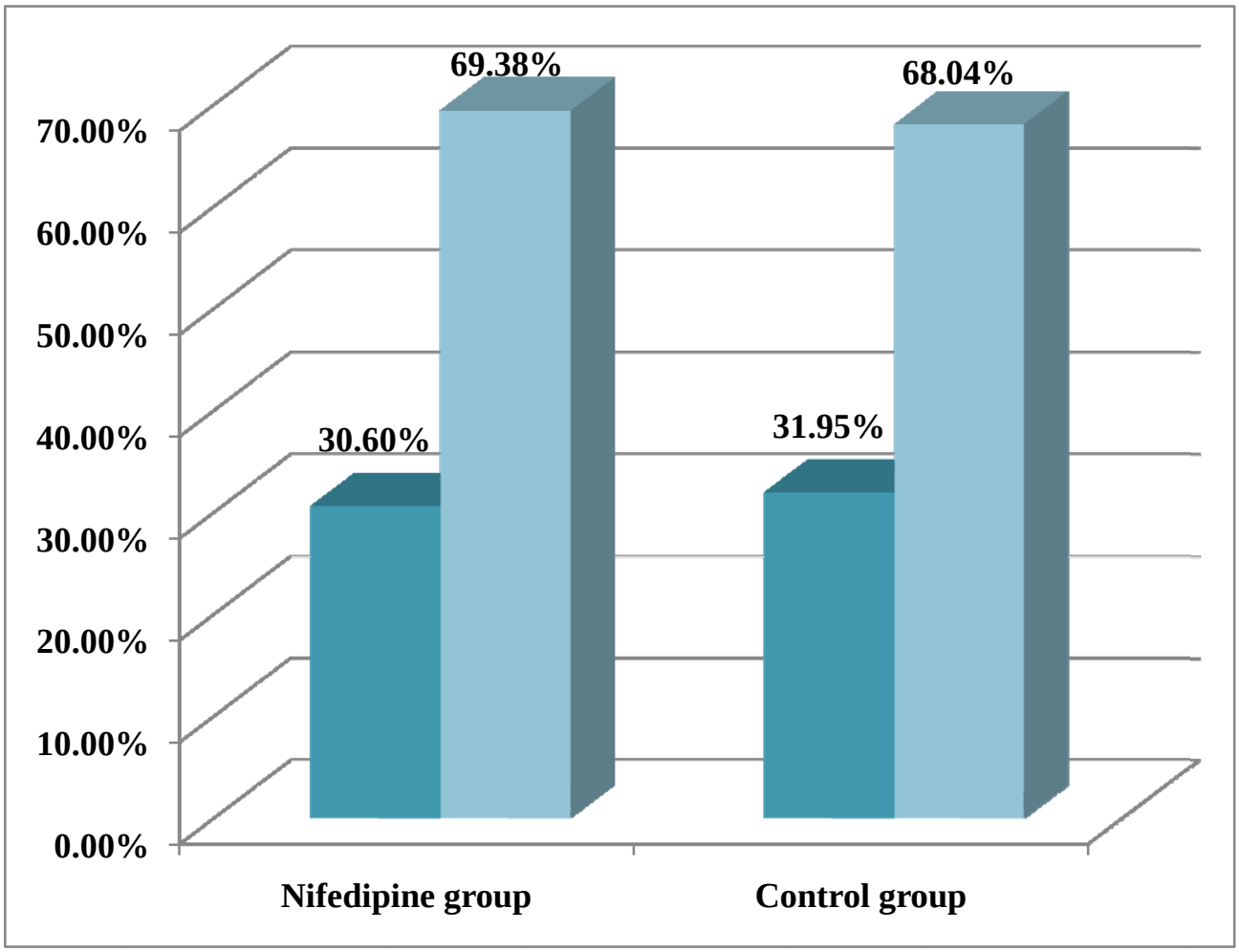
Table: 3



Incidence of preterm labour among primi gravida and multi gravida were 66.1% and 33.8% respectively.

GESTATIONAL AGE

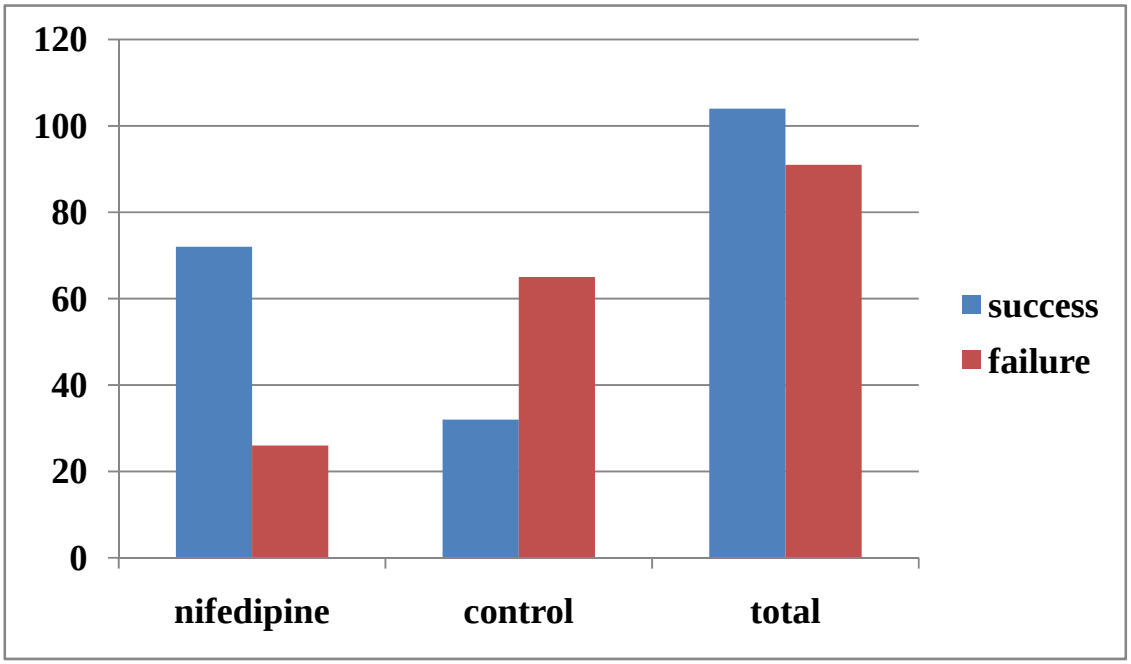
Table: 4



Incidence of preterm labour between 28-30 weeks is 31.28 %and between 31-34 weeks is 68.o4% among both groups

SUCCESS OF TOCOLYSIS

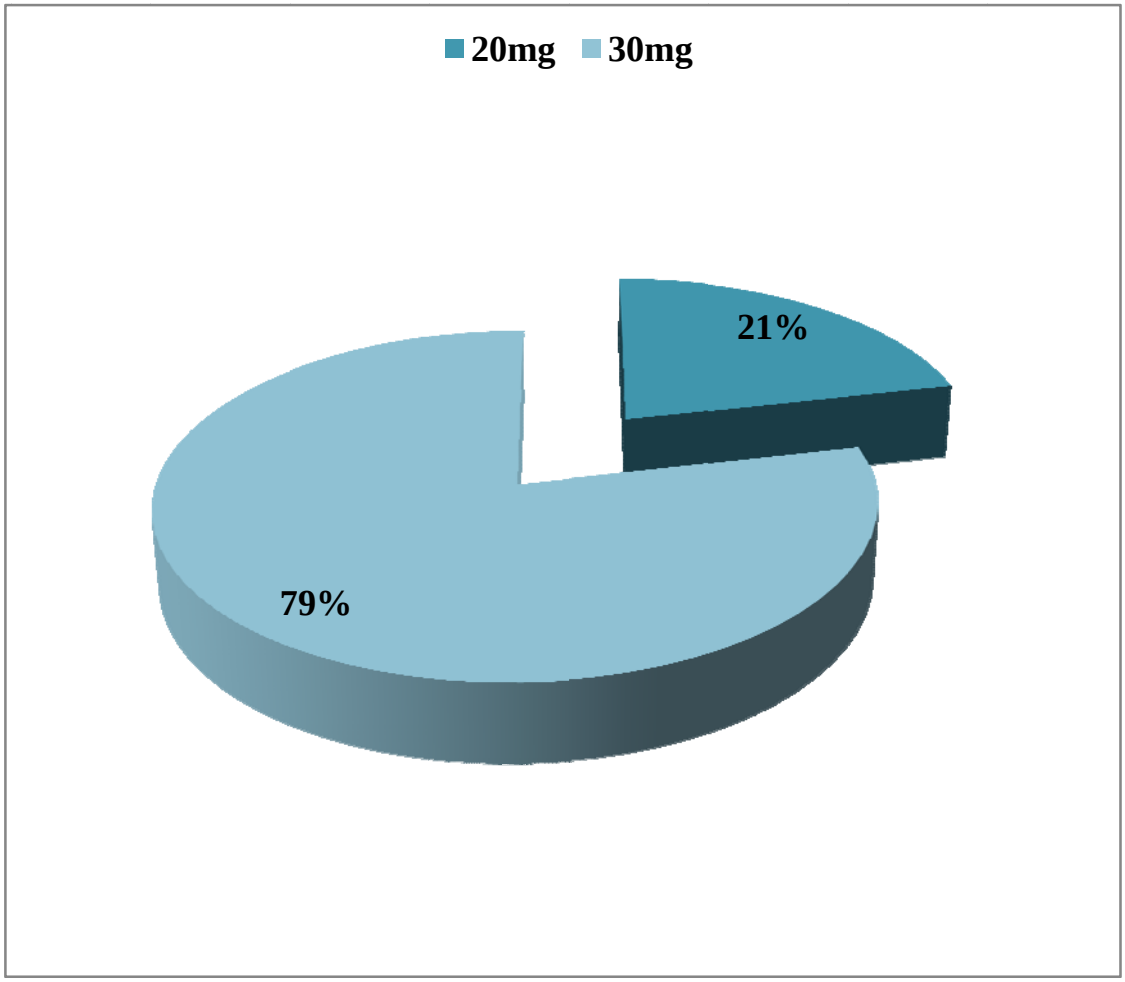
Table: 5



The success in Nifedipine and controls are 73.4% and 32.9% respectively. By test of proportion p value was found to be < 0.001 which is statistically significant.

DOSAGE REQUIRED

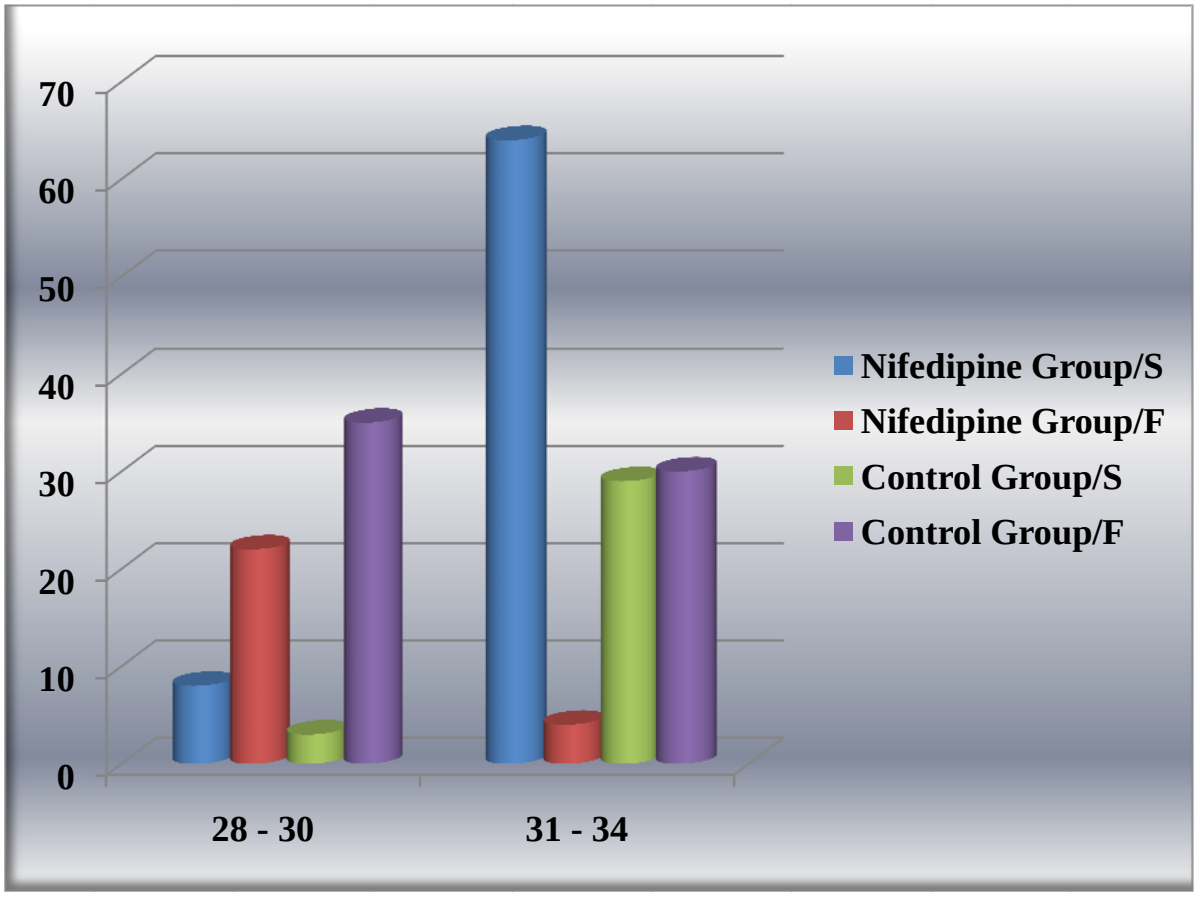
Table: 6



78.57% of patients required 30 mg to suppress uterine contractions whereas 21.4% required 20 mg to suppress uterine contractions.

RESPONSE ACCORDING TO GESTATIONAL AGE

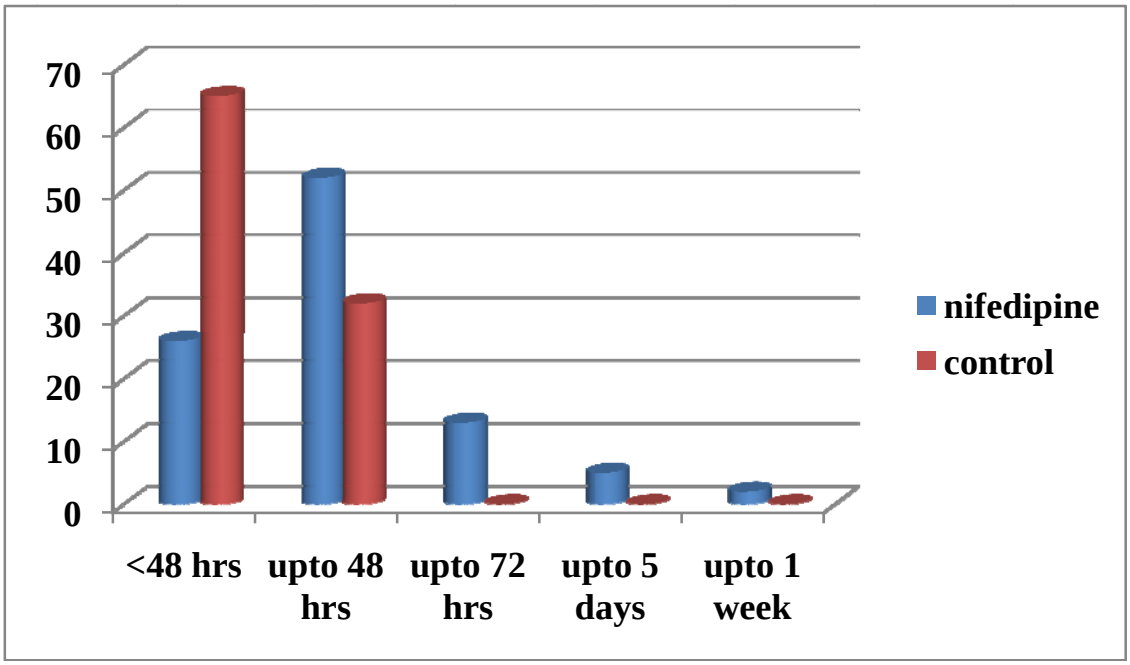
Table: 7



Prolongation of pregnancy more than 48 hours is 88.8% and 90.6% in 31-34 weeks gestational group among nifedipine and control groups respectively .11.1% and 9.3% in 28-30 weeks gestational group are in nifedipine and control groups respectively.

DURATION OF PROLONGATION

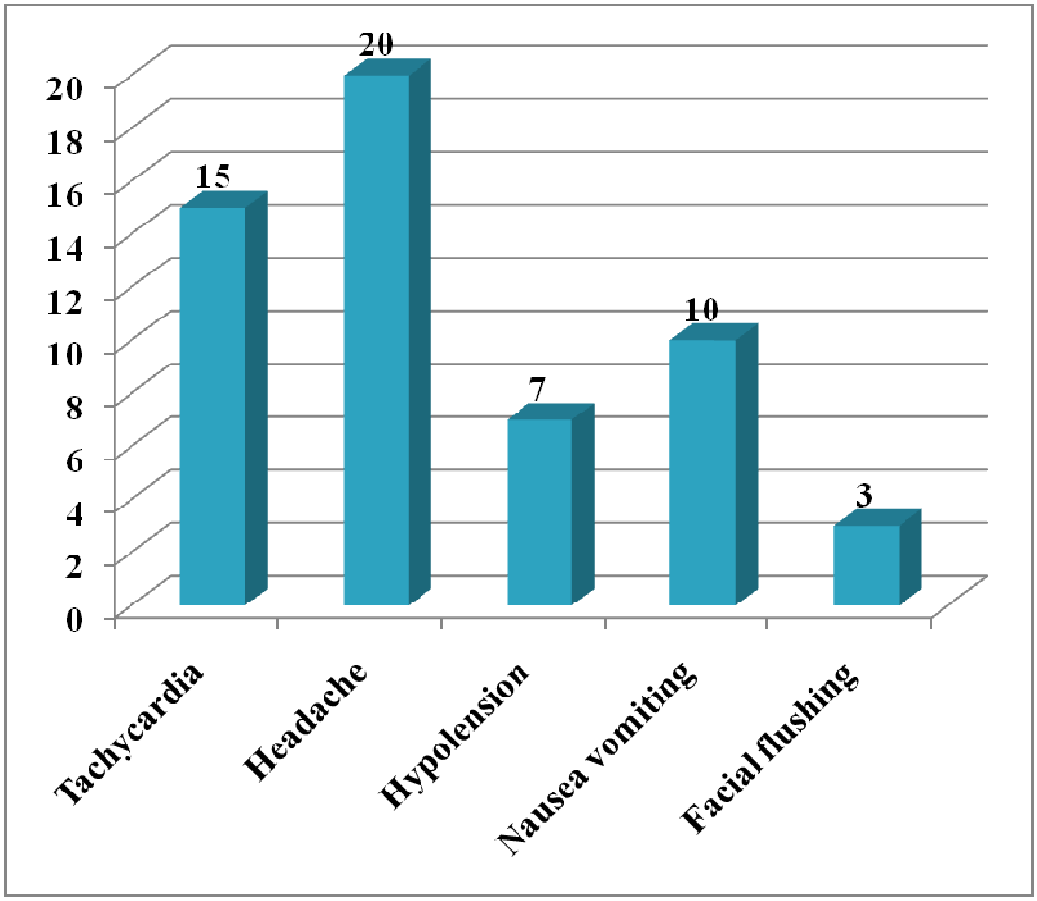
Table: 8



Prolongation of delivery beyond 48 hours was seen in 53.06% in nifedipine group compared to 32.9% in control group. Delivery occurred within 48 hours in 26.5% in nifedipine group compared to 67.01% in control group

SIDE EFECTS OF NIFEDIPINE

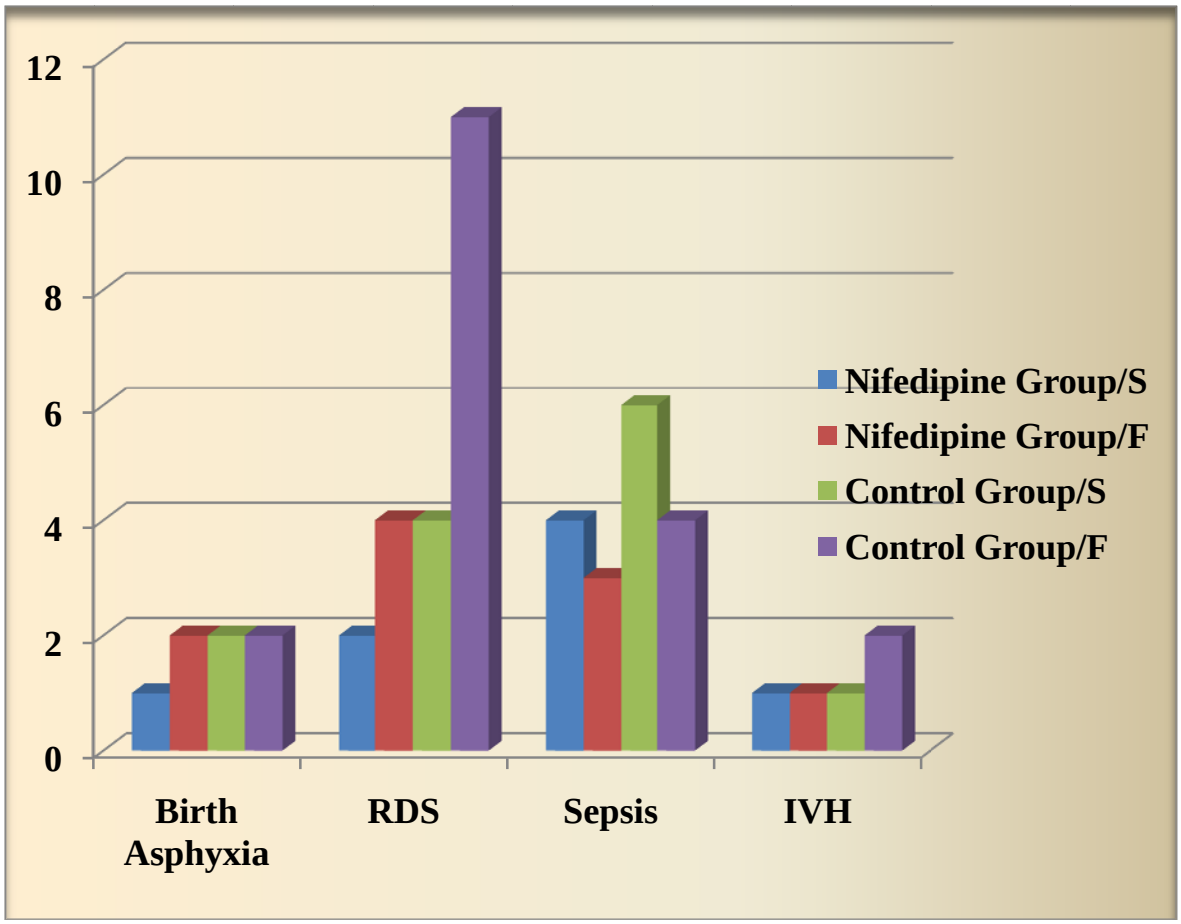
Table: 9



About 56.1% patients had side effects. Headache and maternal tachycardia were commoner among the side effects.

FETAL MORBIDITY

Table: 10

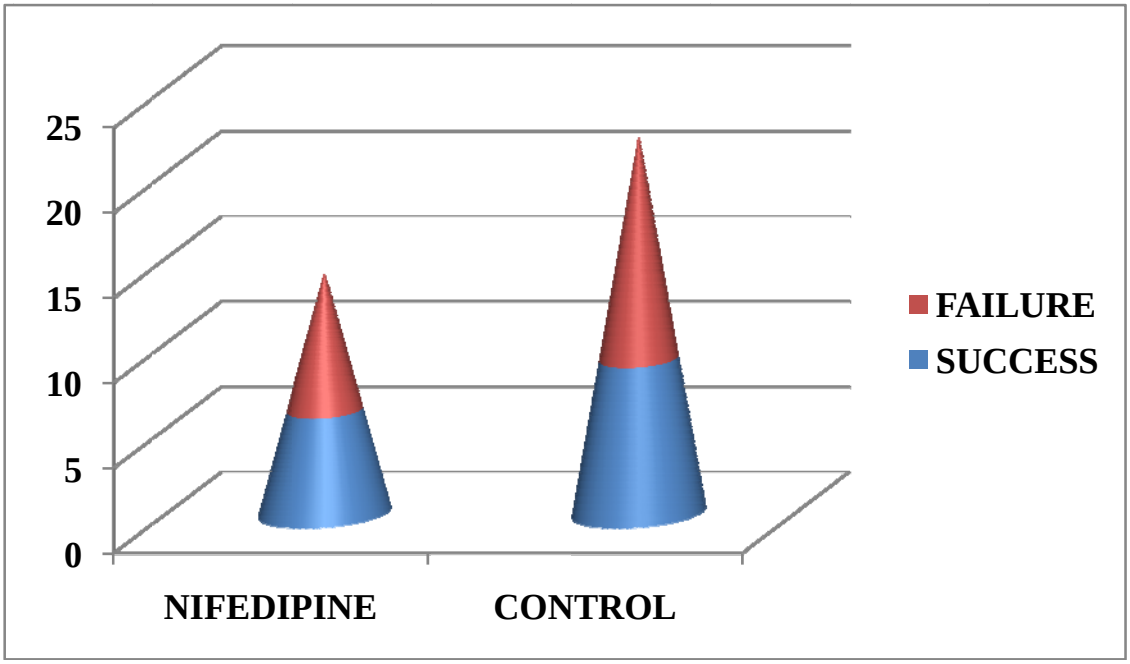


About 11.1 % and 38.46% of neonatal complications occurred in nifedipine success and failure groups respectively.

About 40.6% and 29.23 % of neonatal complications occurred in control success and failure groups.

NEONATAL MORTALITY

Table: 11

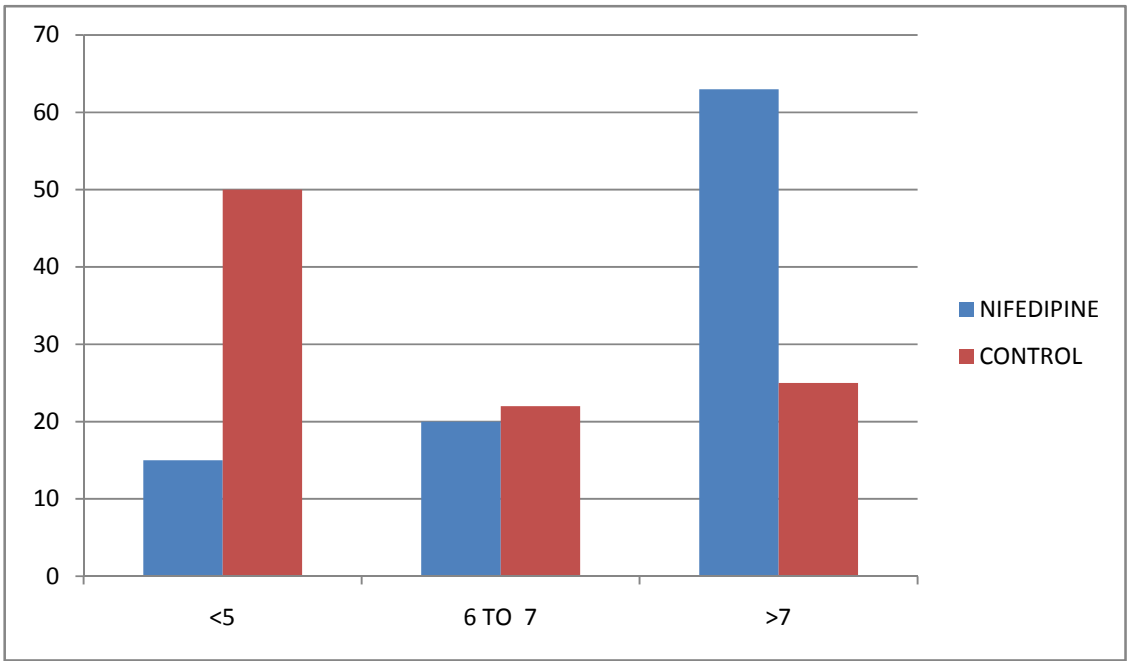


Neonatal mortality was 14.28 % and 22.8.% among Nifedipine and control groups respectively

OVERALL NEONATAL MORTALITY WAS 18.46% AMONG BOTH GROUPS

APGAR SCORE

Table: 12

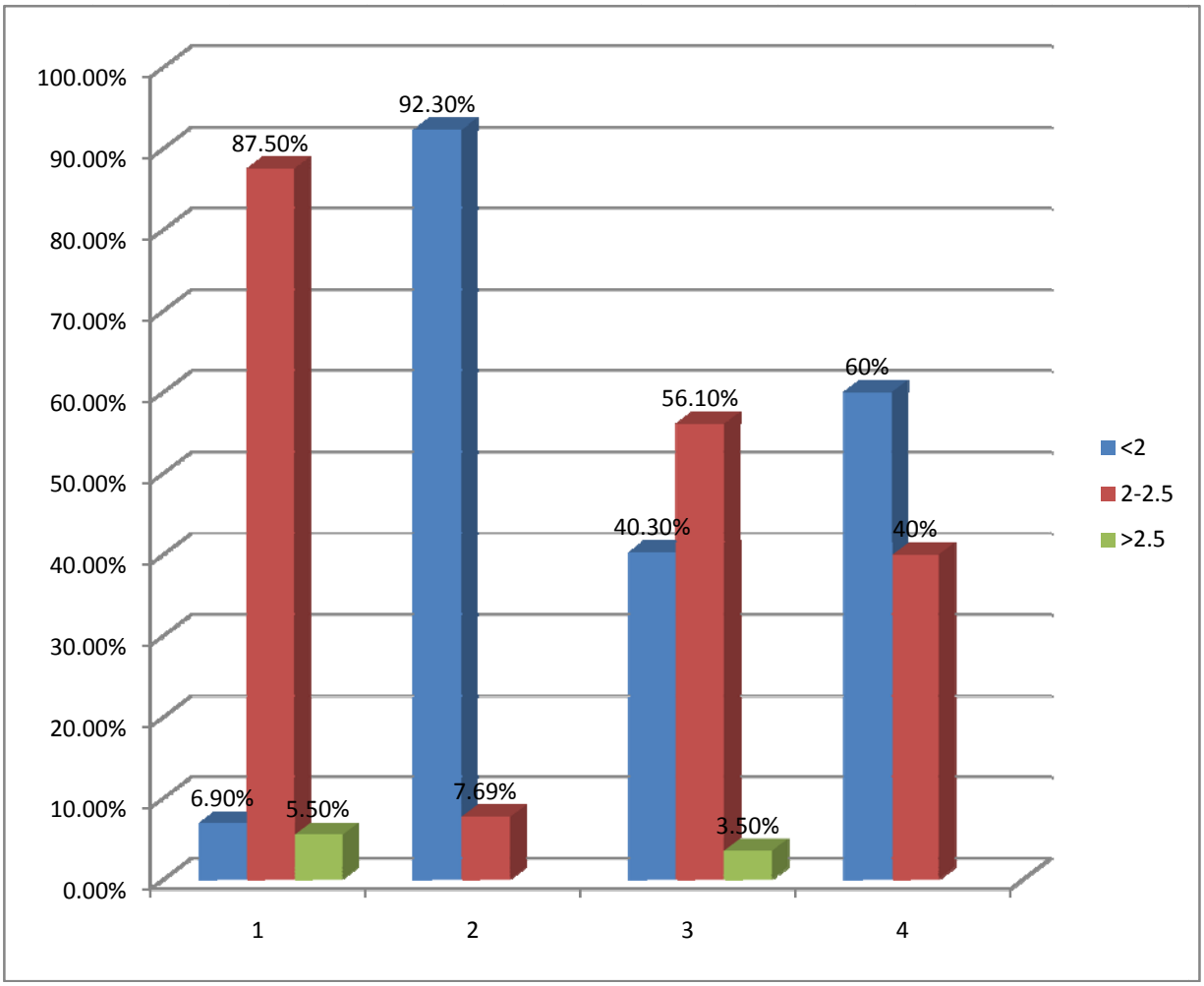


Among the success groups, 73.6% belonged to Nifedipine, 56.2% belonged to control group having apgar >7

P value <0.001 significant.

WEIGHT OF BABY OF BIRTH

Table: 13



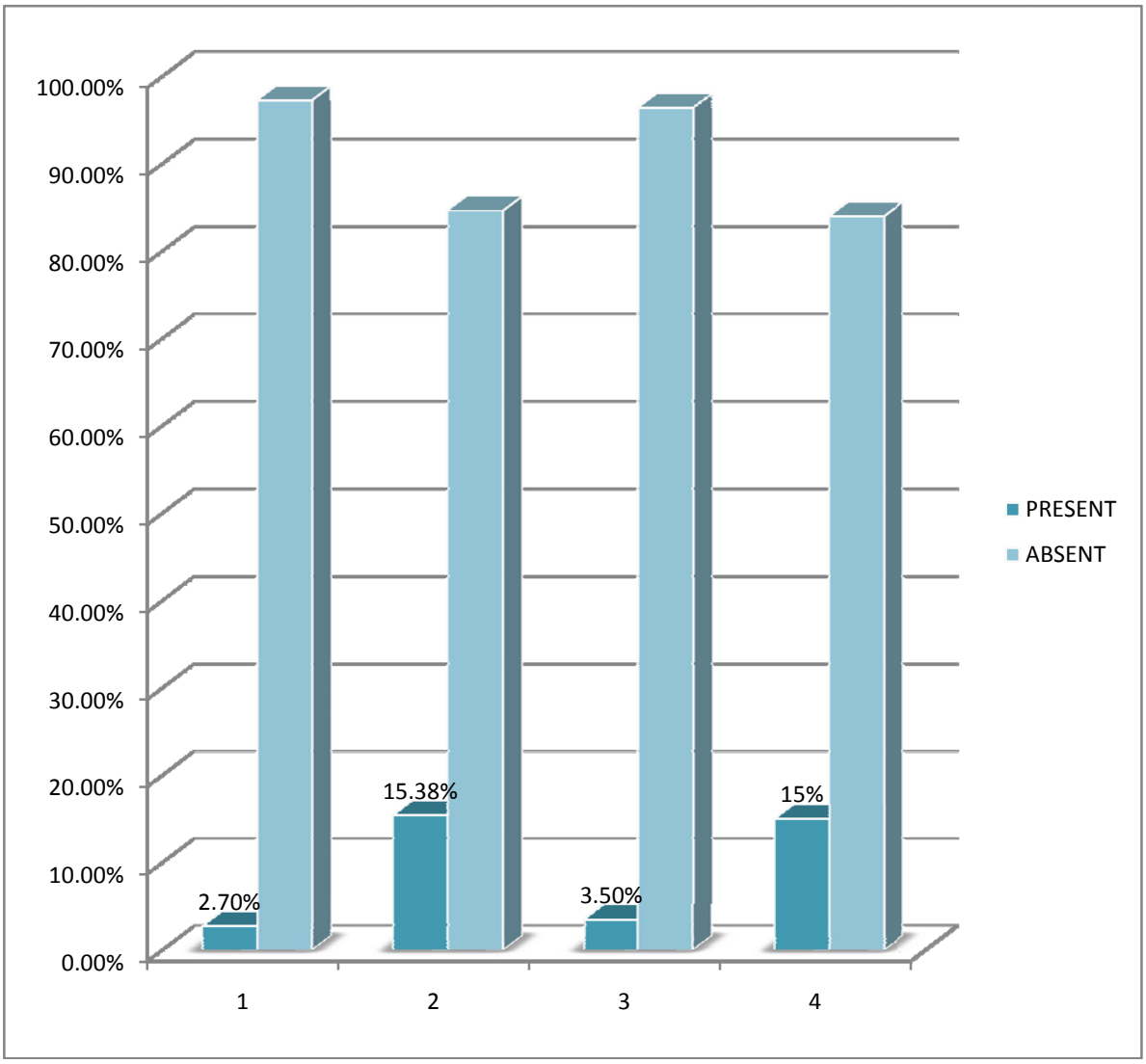
1- Nifedipine success 2- Nifedipine failure 3- Control success 4- Control failure

84.7% cases among Nifedipine success groups had birth weight of 2-2.5 kg when compare with 56.2% in control success group.

8.3% in Nifedipine success group had birth weight >2.5 kg compared to 6.25 in control success groups .p value 0.001 statistically significant.

RESPIRATORY DISTRESS SYNDROME

Table: 14



Incidence of RDS is 2.7% and 15.38% in Nifedipine success and failure respectively, compared to 12.5% and 16.9% in control success and failure groups. P value 0.042.statistically significant.

PROFORMA

Name	Age
IP.No	Unit
Gravida	
Para	Last Menstrual Period (LMP)
Live	Expected Date of Delivery (EDD)
Abortion	Corrected EDD (C.EDD)
SES	Menstrual cycle
Occupation	Height
Residence	Weight

Booked / Unbooked (UB)

Immunized / Not

DOA (Date of Admission)

Duration of Hospital stay

DOD (Date of Discharge)

Period of gestation

Present complaints

Lower abdominal pain

Dull low backache

Vaginal discharge

Fluid leaking per vaginum

Fever

UTI (Urinary Tract Infection)

URI (Upper Respiratory Tract Infection)

Bleeding

Obstetric history

I. Trimester

- Hyperemesis
- Exanthematous fever
- Bleeding
- Radiation exposure
- Medication
- Pain abdomen

II. Trimester

- Date of Quickening
- Bleeding per vaginum
- History of PIH
- H/O GDM (Gestational Diabetes Mellitus)

III. Trimester

Bleeding per vaginum

UTI

Cervico vaginal infection

Coitus

Diabetes

Hypertension

Fever

Trauma

Past obstetric history

Previous child birth

H/O abortion

H/O Preterm labour

H/O babies with congenital anomalies

Past Medical History

Tuberculosis

Bronchial Asthma

STD (Sexually Transmitted Diseases)

Jaundice

Renal disease

Heart disease

Diabetes mellitus

Epilepsy

General examination

Temperature (T) Pallor Pedal edema

PR BP RR RS CVS

Obstetric examination

Per Abdomen:-

Fundal height

Symphysio fundal height

Contractions

Presentation

Position

Liquor

FHR (Fetal Heart Rate)

Expected Fetal Weight at admission

Weight after birth

Per Vaginal Examination (P/V)

Cervix

Membranes

Pelvis

Investigations

Urine analysis

Urine culture sensitivity

Complete Blood Count

Blood urea,

Sugar

S. Creatinine

S. Electrolytes

ECG

USG Abdomen

Nifedipine

Time	Dose	Contraction	T	PR	BP	RR	FHR	P/V

Side effects

Period of tocolysis

Mode of delivery

Fetal Outcome

Birth weight

Apgar

Neonatal complication

NIFEDIPINE GROUP

S.No	Name	Age	IP.No	OBST CODE	GA WKS	B/UB	(cm)Dilatation	Dose	SE	Mode of Delivery	Operation Success	hrs of prolongation	WT in KG	5'A PGAR N/10	Neonatal Complication Mortality
1	Ranjini	21	6602	PRIMI	34	B	3	30	T	V	S	C	2.2	8	
2	Megala	23	3638	G_2A_1	30	B	3	20	N,V	V	F	A	1.7	6	
3	Gowsalya	18	6610	PRIMI	34	B	3	30	Ft	V	S	B	2.3	6	
4	Nithya	21	6638	PRIMI	34	B	3	30	H	V	S	B	2.2	8	1
5	Priyadarshni	28	6820	$G_3P_1L_1A_1$	32	B	3	30	T	V	S	B	2	8	
6	Ponni	20	6230	PRIMI	30	B	2	20	N,V	V	S	D	1.6	5	3
7	Nadiya	27	6719	$G_2P_1L_1$	34	B	3	30	H	V	S	B	2.3	8	2
8	Sathya	26	6002	G_2A_1	34	UB	3	30		V	S	B	2.2	8	
9	Pushpa	22	6125	PRIMI	30	UB	3	20	N,V	V	F	A	1.5	5	1
10	Sumathi	28	6560	$G_2P_1L_1$	34	UB	3	30	T	V	S	B	2.2	8	
11	Selvi	31	6647	$G_3P_1L_1A_1$	34	UB	3	30		V	S	B	2.1	6	
12	Divya	18	6503	PRIMI	34	B	3	30		V	S	B	2.3	8	
13	Vanitha	21	6799	PRIMI	28	B	3	20	T	V	F	A	1.6	5	1
14	Devi	23	6905	$G_3P_2L_1A_1$	30	B	3	30	H	V	F	A	1.7	5	
15	Kavitha	26	6820	$G_2P_1L_1$	34	B	2	30	H	V	S	D	2.4	8	
16	Panchavarnam	21	6250	PRIMI	34	UB	3	30		V	S	B	2.2	8	

17	Ramjan Begum	19	6325	PRIMI	34	B	2	30	H	V	S	E	2.5	8	
18	Saraswathy	27	6973	G2P1L1	32	B	3	20		V	S	B	2.1	8	
19	Esther	32	7010	$G_4P_2L_2A_1$	30	UB	3	30	H	V	F	A	1.5	7	
20	Rani	21	7094	$G_3P_2L_2$	32	B	3	20	T	V	S	B	1.9	6	1
21	Babitha	29	7118	$G_3P_1L_1A_1$	34	UB	3	30		V	S	B	2.3	8	
22	Sangeetha	22	6561	G_2A_1	30	B	3	30		V	F	A	2	7	
23	Hemalatha	18	7091	PRIMI	34	B	3	20		V	S	B	2.2	8	
24	Yamuna	23	7729	PRIMI	34	B	3	30		V	S	B	2.3	8	
25	Jeeva	28	7635	$G_2P_1L_1$	34	UB	3	30		V	S	B	2.1	6	
26	Kavitha	27	7780	PRIMI	28	B	2	30	H	V	S	D	1.6	5	3+
27	Girija	19	10203	PRIMI	32	B	3	20	N,V	V	S	B	2	6	
28	Parvathy	31	8967	$G_4P_3L_1$	34	UB	3	30	T	V	S	B	2.2	8	
29	Thirupurasundari	27	10250	PRIMI	34	B	3	30		V	S	B	2	8	
30	Deepika	22	10295	$G_2P_1L_1$	30	UB	3	30	T	V	F	A	2	7	
31	Pavithra	26	10172	PRIMI	34	B	3	30	Ft	V	S	C	2.3	8	
32	Santhini	24	10332	$G_2P_1L_1$	30	B	3	30		V	S	C	1.5	4	3+
33	Fathima	28	10312	$G_2P_1L_1$	32	UB	3	20	↓BP	V	S	B	2	8	
34	Megala	18	10373	PRIMI	34	B	2	30		V	S	B	2.4	8	
35	Gomathy	22	10413	PRIMI	28	B	3	30	T	V	S	C	1.6	5	2+
36	Keerthana	26	10466	PRIMI	34	B	3	30		V	S	B	2.2	8	
37	Ambiga	30	10362	$G_3P_2L_2$	32	B	2	20	H	V	S	D	1.8	6	2+

38	Nandhini	23	10405	PRIMI	34	B	3	30	T	V	S	B	2.2	8	
39	Lakshmi	27	10501	PRIMI	34	B	2	30	T	V`	S	C	2.3	8	
40	Revathy	19	10521	$G_2P_1L_1$	32	UB	3	30	N,V	V	F	A	1.8	6	2
41	Subalakshmi	28	10581	$G_2P_1L_1$	34	B	3	30		V	S	B	2.2	8	
42	Bhavani	23	10598	PRIMI	34	B	3	20	N,V	V	F	A	2.3	7	
43	Malathy	26	10698	PRIMI	30	B	3	30	T	V	S	C	1.5	6	
44	Thenmozhi	22	10840	$G_3P_1L_1A_1$	30	B	3	30	Ft	V	F	A	1.2	5	2
45	Mahalakshmi	28	10851	PRIMI	34	B	3	30	T	V	S	B	2.2	8	
46	Nandini	17	10791	PRIMI	32	UB	2	30	N,V	V	S	B	1.9	6	
47	Dhanalakshmi	27	10914	PRIMI	32	B	3	20	T	N	S	B	1.8	6	
48	Norrjahan	21	10786	PRIMI	32	B	3	30		N	F	A	1.7	7	1
49	Devi	31	10998	$G_2P_1L_1$	34	B	3	30		N	F	A	2.2	7	
50	Punitha	26	11015	PRIMI	30	B	3	30		N	F	A	1.6	5	+
51	Rekha	29	11017	G2P1L1	34	B	3	20		V	S	B	2.4	8	
52	Rashida	23	11071	PRIMI	34	B	3	30	Ft	V	S	B	2.2	8	
53	Shakila	27	11084	PRIMI	34	UB	2	30	↓BP	V	S	E	2.4	8	
54	Savithiri	21	11138	G_2A_1	30	B	3	20	N,V	V	F	A	1.6	5	2+
55	Divya	27	11150	PRIMI	34	B	3	30		V	S	B	2	8	
56	Vaitheeswari	19	11207	PRIMI	34	B	3	30	T	V	S	C	2.3	8	
57	Kala	25	11193	G2P1L1	28	UB	3	30		V	F	A	1.6	7	
58	Sindu	26	11076	PRIMI	34	B	3	20		V	S	B	2.3	8	

59	Malathy	22	11269	PRIMI	30	B	3	30	H	V	F	A	1.5	5	0
60	Maheswari	28	11080	$G_2P_1L_1$	34	UB	3	30		V	S	B	2.2	8	
61	Taj Begum	21	11243	PRIMI	34	B	3	30	FF	V	S	C	2.3	8	
62	Kalaiarasi	27	11253	$G_2P_1L_1$	30	UB	3	30	↓BP	V	F	A	1.7	7	
63	Egavalli	19	11196	PRIMI	32	B	3	30	T	V	S	B	1.7	6	
64	Reena	23	11247	PRIMI	34	B	3	30	H	V	S	B	2.2	8	
65	Rani	31	11375	PRIMI	28	B	3	30		V	F	A	1.5	4	+
66	Sagayamary	24	2208	$G_2P_1L_1$	32	B	2	30	H	V	S	B	2	6	
67	Nandini	21	12238	PRIMI	34	B	3	30		V	S	B	2.4	8	
68	Shalini	24	12235	$G_3P_2L_2$	32	UB	3	20	H	V	S	B	1.8	6	
69	Mohana	21	12248	PRIMI	30	B	3	30	N,V	V	S	C	2	8	3+
70	Hamsa	22	12331	PRIMI	34	B	2	30	H	V	S	B	2	8	
71	Rajjya	27	12398	PRIMI	34	B	3	30		V	S	B	2.2	8	
72	Lavanya	25	12301	PRIMI	34	B	3	30	H	V	S	B	2.3	8	
73	Shanthi	20	12488	PRIMI	30	B	3	30		V	F	A	1.6	5	3+
74	Chitra	25	12225	PRIMI	34	B	2	30		V	S	B	2	8	
75	Yasoda	24	12599	PRIMI	32	B	3	20	↓BP	V	S	B	1.9	6	
76	Vasanthi	18	12613	PRIMI	30	B	3	30		V	F	A	1.6	5	3+
77	Subhasini	25	12236	PRIMI	34	B	3	30	N,V	V	S	B	2.2	8	
78	Bhavani	25	12593	PRIMI	32	B	2	30	H	V	S	B	2	8	
79	Hemalatha	21	12616	G_2A_1	34	UB	3	30		V	S	B	2.4	8	

80	Radhika	26	12665	G_2A_1	34	B	3	20		V	S	B	2.5	8	
81	Barkath	23	8874	PRIMI	34	B	3	30	FF	V	S	B	2.4	7	
82	Pavithra	28	8887	G2P1L1	32	B	3	30		V	S	C	1.8	6	
83	Amala	26	8984	PRIMI	34	B	3	30		V	S	B	2.2	7	
84	Kalaivani	32	8934	$G_2P_1L_1$	30	B	3	20	H	V	F	A	1.5	7	
85	Sasikala	26	8881	$G_2P_1L_1$	28	B	3	30		V	F	A	1.2	5	4+
86	Menaka	21	8974	PRIMI	34	B	3	30	FF	V	S	C	2.2	8	
87	Ammu	29	9019	$G_2P_1L_1$	32	UB	3	20	H	V	S	B	2.1	8	
88	Ilamathy	23	9077	PRIMI	30	B	3	30		V	S	C	1.4	5	4+
89	Divya	20	9113	PRIMI	34	B	3	30		V	S	B	2.3	8	
90	Gomahy	27	9166	$G_2P_1L_1$	32	UB	2	30		V	S	B	1.8	6	
91	Bhavani	27	9174	PRIMI	34	B	3	30	H	V	S	D	2.4	8	
92	Devi	25	9051	PRIMI	32	B	3	30	↓BP	V	S	C	2.1	6	
93	Abirami	24	9136	PRIMI	30	B	3	30		V	F	A	1.5	7	
94	Kalaichelvi	26	9225	PRIMI	34	B	3	30		V	F	A	2.3	8	
95	Poongodi	29	9025	PRIMI	34	B	3	20	↓BP	V	S	B	2.4	7	
96	Usha	25	9189	PRIMI	30	B	3	30	H	V	F	A	1.9	5	3+
97	Anuradha	26	9409	PRIMI	34	B	3	30		V	S	B	2.2	8	
98	Prema	31	9210	$G_2P_1L_1$	30	UB	3	30	H	V	F	A	1.6	8	

CONTROLS

S.No	Name	Age	IP.No	OBST CODE	B/UB	GA wks	(cm)Dilatation	Mode of Delivery	duration hrs prolongat	S/F	WT in KG	5'A PGAR N/10	Neonatal Complication Mortality
1	Priya	25	6577	PRIMI	B	30	3	V	A	F	1.60	5	2+
2	Gayathri	27	6605	PRIMI	B	34	3	V	A	F	2.30	8	
3	Sasi	21	3639	$G_3P_1L_1A_1$	B	34	3	V	B	S	2.40	6	1+
4	Banupriya	26	6613	PRIMI	B	32	3	V	A	F	1.90	5	2
5	Saranya	23	6559	PRIMI	B	34	3	V	A	F	2.30	6	
6	Jerina Begum	26	6661	PRIMI	B	30	3	V	A	F	1.70	5	
7	Ambiga	24	6682	PRIMI	B	34	3	V	B	S	2.40	5	2+
8	Shantha	23	9842	$G_2P_1L_1$	B	34	3	V	B	S	2.40	5	2+
9	Jailani	22	6742	G_2P_1L0	B	28	3	V	A	F	1.40	5	4+
10	Amulu	27	6625	PRIMI	B	34	3	V	B	S	2.50	6	1+
11	Aishwarya	26	9804	$G_2P_1L_1$	B	30	3	V	A	F	1.70	5	2
12	Maheswari	28	6812	$G_2P_1L_1$	UB	30	3	V	A	F	1.80	5	
13	Radika	24	6771	PRIMI	B	34	3	V	A	F	2.30	8	
14	Sasikala	23	6778	PRIMI	B	34	3	V	A	F	2.25	6	
15	Rajeshwari	28	6875	$G_2P_1L_1$	B	32	3	V	A	F	1.90	5	2

16	Jhansi	22	6865	PRIMI	B	30	3	V	A	F	1.70	5	2
17	Rekha	23	6925	PRIMI	UB	32	3	V	A	F	1.90	6	
18	Priya	26	6205	PRIMI	B	30	3	V	A	F	1.80	5	
19	Mary	25	7054	$G_2P_1L_1$	B	32	3	V	A	F	1.90	5	
20	Sangeeta	24	6561	G_2A_1	UB	34	3	V	B	S	2.40	7	
21	Selvi	23	7015	PRIMI	B	30	3	V	A	F	1.70	5	2
22	Devi	27	7241	$G_3P_1L_1A_1$	B	32	3	V	A	F	2.00	6	
23	Mary	29	7054	$G_2P_1L_1$	B	33	3	V	A	F	2.10	6	
24	Saraswathy	31	6973	PRIMI	B	34	3	V	B	S	2.40	6	2
25	Esther	26	7010	PRIMI	UB	28	3	V	A	F	1.50	5	1+
26	Tamilselvi	28	7151	$G_3P_1L_1A_1$	B	30	3	V	A	F	1.80	8	2
27	Gomathi	24	7736	PRIMI	B	34	2	V	B	S	2.40	8	2
28	Kowsiya	23	7795	PRIMI	B	34	3	V	A	F	2.30	6	
29	Gunasundari	31	10246	$G_2P_1L_1$	B	30	3	V	A	F	1.70	5	2+
30	Monika	26	10244	PRIMI	B	34	3	V	B	S	2.40	6	
31	Saraswathy	28	10194	G2P1L1	UB	32	3	V	A	F	2.10	6	
32	Bhavani	24	10346	PRIMI	B	34	3	V	B	S	2.40	8	3
33	Elakiya	27	10343	$G_2P_1L_1$	B	30	3	V	A	F	1.70	5	1+
34	Anjali	19	10357	G2P1L1	UB	32	3	V	A	F	2.00	6	
35	Gunasundari	28	10355	$G_2P_1L_1$	B	34	3	V	B	S	2.30	6	3

36	Jyothy	23	10409	PRIMI	B	30	3	V	A	F	1.60	5	
37	Nagavalli	26	10437	G_2A_1	B	34	3	V	B	S	2.40	7	
38	Jerina	22	10370	PRIMI	B	34	3	V	A	F	2.30	5	
39	Megala	19	10330	PRIMI	B	30	3	V	A	F	1.70	5	
40	Priya	27	10267	$G_2P_1L_1$	B	34	3	V	B	S	2.30	4	3+
41	Soniya	26	10530	PRIMI	UB	33	3	V	A	F	2.00	7	
42	Amudavalli	21	10607	PRIMI	B	32	3	V	A	F	2.00	7	
43	Amudha	28	10147	PRIMI	B	30	3	V	A	F	1.60	5	
44	Bhuvaneshwari	23	10738	PRIMI	B	32	3	V	B	S	1.90	5	3+
45	Latha	27	10845	PRIMI	B	30	3	V	A	F	1.70	4	
46	Selvi	22	10799	PRIMI	UB	34	3	V	B	S	2.30	7	
47	Seetha	24	10811	PRIMI	B	32	3	V	B	S	1.90	5	
48	Priya	17	10928	PRIMI	B	30	3	V	A	F	1.60	5	
49	Devi	18	10932	PRIMI	B	32	3	V	B	S	2.10	5	3+
50	Karpagam	26	10975	$G_2P_1L_1$	B	30	3	V	B	S	1.80	5	3+
51	Deepa	28	10998	$G_2P_1L_1$	B	34	3	V	B	S	2.30	8	
52	Jennifer	23	10956	PRIMI	B	30	3	V	A	F	1.90	5	
53	Anitha	19	11039	PRIMI	B	34	3	V	B	S	2.40	8	
54	Ambika	23	11117	PRIMI	B	34	3	V	B	S	2.50	7	
55	Kanchana	19	11134	PRIMI	B	28	3	V	B	S	1.50	5	

56	Malar	27	112256	$G_2P_1L_1$	B	30	3	V	A	F	1.60	5	
57	Rosy	23	11106	PRIMI	UB	34	3	V	B	S	2.30	7	
58	Vasanthi	28	11266	$G_2P_1L_1$	B	34	3	V	B	S	2.40	8	
59	Sheela	32	11236	$G_2P_1L_1$	B	34	3	V	B	S	2.30	7	
60	Shakeena	21	11234	PRIMI	B	30	3	V	A	F	1.90	7	
61	Pandipriya	26	11260	G2P1L1	B	32	3	V	A	F	2.00	8	
62	Sakira	18	11361	PRIMI	B	34	3	V	B	S	2.30	5	
63	Mini	19	11385	$G_2P_1L_1A_1$	UB	32	3	V	A	F	1.90	6	
64	Bhuvaneshwari	27	11393	G2P1L1	B	34	3	V	B	S	2.30	8	4
65	Suganya	19	12186	PRIMI	B	32	3	V	A	F	2.00	5	
66	Barathi	19	12239	PRIMI	B	34	3	V	A	F	2.20	5	
67	Sareen	27	12082	PRIMI	UB	32	3	V	A	F	2.00	7	2+
68	Bakya	22	12195	G_2A_1	B	32	3	V	A	F	1.90	5	
69	Suganya	26	12320	G_2A_1	B	30	3	V	A	F	1.60	5	2+
70	Priya	18	12265	$G_2P_1L_1$	UB	34	3	V	A	F	1.90	6	
71	Mariammal	24	12389	G2P1L1	B	30	3	V	A	F	1.60	4	
72	Aishwarya	18	12453	PRIMI	UB	32	3	V	A	F	1.90	5	
73	Vedavalli	31	12465	$G_2P_1L_1$	B	30	3	V	A	F	1.60	5	
74	Sujitha	22	12522	PRIMI	B	34	3	V	B	S	2.40	8	
75	Indumathy	26	12552	$G_3P_1L_1A_1$	B	34	3	V	B	S	2.30	7	

76	Lakshmi	18	12612	PRIMI	B	34	2	V	B	S	2.30	8	
77	Nalini	24	12474	PRIMI	B	32	2	V	A	F	2.00	5	+
78	Gayathri	19	15573	$G_2P_1L_1$	B	34	3	V	B	S	2.20	8	
79	Betisda	22	12672	PRIMI	B	32	3	V	A	F	1.90	8	
80	Kavitha	24	8774	PRIMI	B	30	2	V	A	F	1.70	5	0
81	Selvi	30	8726	$G_3P_1L_1A_1$	B	34	3	V	B	S	2.40	7	
82	Madhuri	21	8919	G_2A_1	B	30	3	V	A	F	1.70	4	4+
83	Solaiyammal	23	8931	PRIMI	B	34	3	V	B	S	2.20	7	
84	Mohana	31	8984	$G_4P_1L_1A_2$	B	28	2	V	A	F	1.40	5	4+
85	Amuda	21	8974	PRIMI	B	32	3	V	A	F	2.00	8	3
86	Anbu	22	8118	PRIMI	B	34	3	V	A	F	2.30	8	
87	Krithika	24	9070	G2P1LI	B	32	3	V	A	F	2.00	7	3+
88	Priyanka	17	9095	PRIMI	B	30	3	V	A	F	2.00	7	
89	Sandhya	24	9044	PRIMI	B	32	3	V	A	F	2.10	7	
90	Revathy	21	9165	PRIMI	B	33	3	V	A	F	2.20	5	3+
91	Elakiya	18	9178	$G_2P_1L_1$	B	32	3	V	A	F	2.30	8	
92	Maheswari	32	9202	$G_2P_1L_1$	B	30	3	V	B	S	1.60	5	
93	Archana	23	9179	$G_2P_1L_1$	B	32	3	V	A	F	2.00	5	
94	Rumeena	25	9047	PRIMI	B	34	3	V	A	F	2.20	7	
95	Sridevi	23	9236	PRIMI	B	32	3	V	A	F	2.10	5	3+

96	Lakshmi	31	9233	$G_2P_1L_1$	B	30	3	V	A	F	1.60	5	
97	Sudha	22	9063	PRIMI	B	32	3	V	A	F	1.90	5	

G - Gravida P - Para L - Life A - Abortion GA - Gestational Age

Wt - Weight B - Booked UB - Un booked S - Success F - Failure V - Vaginal Delivery

HR - Heart rate T - Tachycardia H - Hypotension FF - Facial Flushing

N,V - Nausea Vomiting + Neonatal Mortality 1 - Birth asphyxia 2 respiratory Distress Syndrome

3 - Septicemia 4 - Intra ventricular Haemorrhage

A - Delivery less than 48 hours B - Delivery at 48 hours C - Up to 72 Hours

D - Up to 5 days E - Up to 1 Week